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A RECORD OF THE PROGRESS OF PHARMACY AND THE ALLIED SCIENCES

PUBLICATION COMMITTEE

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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 94. MARCH, 1922. NO. 3.

EDITORIAL

THE ALCOHOL QUESTIONNAIRE.

At great expense and trouble, *The Journal of the American Medical Association* has lately completed a questionnaire to obtain the opinions of the principal portion of the medical profession in the United States on the therapeutic value of the more important alcoholic beverages. The results are not overwhelming in any direction, but the majority against the value of beer and wine for medicinal purposes is very decided. That the interpretation of statistics requires great caution is well known to all who have studied their use. One is frequently inclined to agree with the cynical Frenchman who said that nothing can lie worse than figures except facts.

Over fifty thousand question papers were sent out, of which somewhat more than one-half were returned. This is a disappointing point in itself. A stamped addressed envelope was enclosed, and the answering of the question could hardly require ten minutes for most physicians, who must have formed their opinions already, yet many thousands did not take the trouble even to give this time to one of the most important problems that is now before the medical profession of this country. Of those that answered, the general trend is about the same all over the country, but as might be expected the large cities and the well populated industrial sections of the Atlantic slope show a strong feeling in favor of alcoholic beverages, though even in these beer and wine have more opponents than friends.

Whisky finds the greater favor among those who regard alcohol as useful in disease. This is in accordance with sound therapeutics, for if a powerful drug is to be used at all, it is best to use it in as concentrated a form as is fairly safe and in as definite strength as

it can be obtained under ordinary conditions. This is the reason that morphine sulphate is used instead of opium, quinine sulphate instead of bark, strychnine sulphate instead of nux vomica. Whisky represents a strong, nearly pure and fairly constant preparation of alcohol, and when properly aged has a color and aroma that makes it acceptable, indeed, too acceptable, to many. The ideal method of treatment would be to use the so-called "silent spirit" properly diluted, and, if necessary, flavored acceptably, but psychic problems come into play largely in such lines and physicians have never been favorable to getting back to such simple principles as prescribing alcohol for itself alone.

The large majority against beer and wine has some bearing, although not very much upon one of the questions that have arisen under the Volstead Act. Many persons who are favorable to the restriction of the so-called "strong drinks," whisky and brandy and their many fancy mixtures, believe sincerely that the sale of the beverages of low alcoholic content should be permitted, as they are supposed not to lead to drunkenness. The practical problem is, however, how to prevent the sale of the stronger drinks in the places where the weaker ones are on sale. All experience shows that few of those who keep places for the sale of any form of liquor can be trusted to keep within the law when high profit is the reward of breaking it. The saloon has been a focus of law-breaking from the plains of Mesopotamia in the morning twilight of civilization to the present day, and there seems to be no way to exterminate its evils than complete suppression. To permit the sale of light wines and beers is simply to open the door to the free sale of all other beverages of alcoholic content.

The mere figures of the questionnaire do not give the information necessary to determine accurately the feeling of the more authoritative and better-informed of the profession. While the number of replies is disappointingly less than was hoped, there was still a very considerable return, and the opinions are collected from all sections of the country. As noted above, and as might be expected, the larger cities and industrial areas have the strongest tendencies to favor alcohol. This is probably due in considerable measure to business influences, that is, to the profit which results from the sale of such products, for there can be little doubt that in the large cities many doctors are either openly or secretly interested in drug stores, and the

liability of these to favor conditions which will give them a free hand is too evident to be overlooked or minimized.

After all, when we consider the comparative suddenness with which the nation took up prohibition, the rather drastic regulations which the Volstead Act imposed, the large number of persons who look upon alcoholic beverages as harmless in what is called, (without being clearly defined), "moderation," and the long and extended use it has had in medical practice, the narrow escape from negation which the favorite form—whisky—had, and the very heavy vote against the other forms, it appears that a very large number of active and experienced physicians are not convinced that alcohol has sufficient therapeutic value to make it worth while for the nation to run the risk of its sale. We may consider that the JOURNAL has done a great public service and has thrown considerable light upon the national attitude towards the eighteenth amendment.

Another point, however, deserves consideration. As just stated, many physicians (15,218 to be exact) expressed the view that alcohol is not needed in the treatment of disease, for the exclusion of whisky must be regarded as practically the exclusion of alcohol in any form. Yet alcohol is a powerful drug, capable of influencing certain bodily functions, and the most used drugs, such as morphine, mercurials, arsenicals, strychnine, quinine, are all potent and more or less directly poisonous. Is alcohol alone of all the common potent remedies without therapeutic value? If so, one would like to know the reason. The question must arise as to how many of those who pronounced absolutely against all use of alcohol in treatment were influenced by the perils that it carries with it, and felt that the only escape from evils was complete abandonment of the use of the drug. That alcoholic beverages are used to a very great extent when no necessity for such use exists is evident to everyone, but it still seems to be a question as to whether there is a legitimate field for its employment, though it is probable that this field is much more limited than is commonly assumed, and that the extent to which alcohol is abused is largely due to the laxity of the medical profession on the subject.

H. L.

ORIGINAL PAPERS

PERFUMERY AND COSMETICS.

By E. Fullerton Cook.*

In the cultural development of civilization one of the qualities which lifts mankind above other living things is that esthetic sense of mind and spirit which is expressed by the so-called "fine arts."

To those who will to see are given the delight of nature's glories expressed in mountain, sunset and sea, and in a thousand other beautiful pictures. Man, in sculpture, painting, textile arts, and architecture, has also learned to create beauty and to delight in it. For the ear, great artists have sung their melodious dreams, perpetuating them in music for the stirring of the human heart; for the lifting of nations into realms of sheer delight, or inspiring them to noble deeds. The epicurean artist has brought beauty and joy by his creations. Through the touch of silk and velvet, another sense has brought to man an appreciation of the beautiful. Truly it was ordained that the sense of smell should also bring its gifts; for what more delightful than the perfume-laden air which drifts across a field of new mown hay, or the odor of the pine woods, or the faint perfume of a rose or other fragrant flower.

The enjoyment of fine odors has not received the cultivation that is given music, or painting, or the textile arts; yet it plays an important role in the lives of most of us, influencing our actions and giving to us pleasures, or perhaps distress. Perhaps, however, I have but expressed masculine ignorance of the extent to which the feminine mind has studied and applied this art to which "mere man" is so susceptible.

Piesse records the historic fact that in 1770 an act was introduced into the English Parliament which read:

"That all women of whatever age, rank, profession, or degree, whether virgins, or widows, that shall, from and after such Act, impose upon and betray into matrimony any of his Majesty's subjects, by the scents, paints, cosmetic washes, artificial teeth, false hair, Spanish rouge, iron stays, high-heeled shoes, bolstered hips, shall in-

*Delivered as one of a series of Free Popular Lectures at the Philadelphia College of Pharmacy and Science.

cur the penalty of the law now in force against witch craft and like misdemeanors, and that the marriage, upon conviction, shall stand null and void."

What one among us has not felt the power of that distinctive perfume which means a presence or a precious memory? What woman does not know the advantage of associating a romance with a pleasing perfume and then perpetuating its memory by allowing the capture of a glove or lacy handkerchief which bears the perfume?

Some one has said that no sense brings so vividly to mind its associations as that of smell; perhaps each one of you can bear testimony to this truth.

You who cater to the feminine taste in perfumes should know these facts. It is the distinctive odor, obtainable in every form, suitable for use among the lingerie, for perfuming the bath, or perhaps ready to delicately permeate a room with its sweetness, that will please "my lady."

For this is needed the artists' touch, imagination and the product of the master perfumer.

Perfumes are associated in the earliest records with religious ceremonies. It is but natural that the nations of the Far East, even in extreme antiquity, should have offered the sweet-smelling woods and resins of their native land as gifts to their Gods. Thus did they show their homage and respect.

Upon the Egyptian Sphinx which formed the end of a temple, is pictured the king burning incense and offering a libation of oil or ointment.

In Greek mythology men are pictured as obtaining their knowledge of perfumes through the indiscretion of a nymph of Venus.

The early use of perfumes in the worship of the Hebrews is indicated by many passages of the Bible, and in the thirtieth chapter of Exodus, Moses is directed to burn perfumed gums and woods upon an altar, and Aaron to "burn thereon sweet incense every morning"; Moses is directed also to "take sweet spices, stacte and onycha and galbanum, these pure spices with frankincense," and to "make perfume, a confection, after the art of the apothecary, tempered together, pure and holy," and "whosoever shall make like unto that, to smell thereto, shall even be cut off from his people."

India and Arabia have traditionally been the lands of perfumes and the Greeks, and later the Romans also became devotees of the

perfumers' art, soon adapting it to their personal use and carrying the practice to an extreme never since attempted.

In Greece the perfumer's shop was the common meeting place for gossip, and a Greek poet of 350 B. C. wrote:

"For he t' annoint himself
Dipped not his finger into alabaster,
The vulgar practice of a former age;
But he left fly four doves, with unguents drenched,
Not of our sort, but every bird a perfume bore,
Peculiar, and, differing from the rest;
And they hov'ring around us, from their heavy wings
Showered their sweets upon our robes and furniture,
And I—be not too envious, gentlemen,—
I was bedewed with violet odours."

In the Roman Amphitheatre during a spectacle the air was constantly refreshed by the playing of fountains of perfumed waters.

Perfumed ointments were kept in highly ornamented boxes usually made of alabaster or onyx, and a treatise on the perfumer's art, written by Apollonius, is still extant and gives the sources of supply and the uses of the various odors.

A perfume invented by Frangipanni, one of the earliest Roman nobles, is yet used and bears his name. It is a sachet composed of equal parts of "every known spice," to which is added a weight of orris root equal to the whole, and one per cent. of musk and civet.

It is supposed that the Crusaders brought the perfumer's art to England from Eastern Lands, and by the Elizabethan period it had been developed to a high degree of perfection.

Beau Brummell, the arbiter of English fashion, did not believe in men of fashion using perfumes, and recommended that they send their linen to be washed on Hampstead Heath.

At the close of the nineteenth century, the manufacture of perfumery has been well established; immense laboratories were built in France and England, and their products sold throughout the world.

The raw materials available at that time were all from national sources. A number of animal products had come into use, not for their value as perfumes, but to perform a necessary function in the perfume, namely to retard the lavish expenditure of odor

which the plant or product would otherwise freely give until exhausted.

This class of products are termed "fixatives," and include such substance as musk, ambergris, civet and castor. These materials are still used, although musk and ambergris are scarce and expensive, and synthetic products have successfully replaced them in many instances.

Naturally perfumed woods or flowers represent another class of natural products used throughout the centuries, and still employed for sachets. The most important available today are sandalwood, orris, rose petals, cassie flowers, orange flowers and vertivert.

The Oleoresins of Siam Benzoin, of Oak Moss, Peru Balsam, Tolu Balsam, Galbanum, Orris, Styrax, etc., are another type of preparations which are still used.

The perfume of flowers, fruit and other natural products is due chiefly to a substance called volatile oil. This oil exists in the tissues of the plant, and its extraction is accomplished by one of several ways. Some oils, notably those of the citrus group, including orange and lemon, are found in comparatively large cells, near the surface of the rind, and may be readily removed by one of the following processes:

Sponge Method: The fruit is cut in half, the pulp removed, and the half rind pressed against a sponge which absorbs the liberated oil.

The *"l'cuella process"* is also employed. The fruit is rotated rapidly in a bowl-shaped, tinned-copper vessel, covered inside with small spikes or knives, and the oil which flows from the ruptured oil cells is collected through an opening at the bottom of the bowl.

The latest method of extraction is called the *Thermo-Pneumatic*. The whole fruits are rotated in a cylindrical vessel containing a small amount of water and lined with small spikes, and at the same time steam is admitted or the material heated by the use of a steam jacket. The oil is collected by aspirating or drawing off the vapors through a condenser. Sometimes the oil has been extracted by volatile solvents and separated by means of a vacuum still.

Other volatile oils may readily be obtained by what is termed *"steam distillation."* The oil-bearing portion of the plant, whether fruit, seed, flower or herb is placed in a basket in a still. Water is added and the mixture heated, the vapor being condensed and collected in a Florentine receiver. This vessel is so arranged that the oil may separate and rise to the surface for collection, while the saturated water is drawn off at the bottom. The water thus obtained is sometimes of commercial value, as Orange Flower Water and Rose Water, but, if not salable, it is returned to the still for the next operation, and thus the loss of oil avoided.

The modern still for valatile oils is often adjusted for the use of a vacuum, that the temperature may be reduced.

The more important oils made by this process, and of value to perfumery are Rose, Neroli, Lavender Flowers, Bay, Cardamon, Cinnamon, Rose-Geranium, Jasmine, Orris, Palmarosa, Petit-grain, Sandalwood, Ylang Ylang.

Some volatile oils, especially the more delicate flower perfumes, cannot be obtained successfully by steam distillation, either because the oil exists in minute quantity or is injured by the heat, oxidization or perhaps hydrolysis.

Other processes have therefore been devised. One of these is termed *"Enfleurage"* or the "absorption method."

A mixture of specially selected and highly purified lard and beef fat is spread in a thin layer on a glass plate in a frame, and the fresh flowers, each morning for thirty days, are sprinkled on the fat, the frames being stacked on each other for the intervening time that the odor may be obsorbed. The fat or "pomade" as it is termed is later washed with alcohol to remove the perfume, and these essences were for many years the most important perfume material available.

The flowers best extracted by the enfleurage process are:

Jasmine,
Tuberose,
Jonquil,
Lily of the Valley,
Mignonette (Reseda),
and pomades of Rose, Cassie, Violet, Orange Flowers, Lilac and Heliotrope are also obtainable.

The maceration or infusion process is also employed for this same group, the fresh flowers, each day, being tied in linen bags and macerated in the warmed fat for twenty-four hours, the flowers being removed by centrifuges. The fat should be exposed to at least fifteen different lots of flowers.

This group, which cannot be so satisfactorily heated, are also extracted by cold, *volatile-solvents,* chiefly ether or petroleum ether, and after extraction the solvent is removed by vacuum distillation. By this process are formed what are called "concretes."

The flowers satisfactorily treated by this method are:

Rose,
Parma Violets,
Victoria Violets,
Orange Blossoms,
Jasmine,
Tuberose,
Jonquil,
Cassie,
Mignonette,
and sometimes
Carnations,
Lily of the Valley,
Heliotrope,
Elder Flowers,
Narcissus,
Mimosas.

The volatile-solvent method of extraction removes not only the volatile oil, but also the flower waxes and other inert constituents. If these are now removed, a still more concentrated product results, commercially sold under various names such as "Hyper-essences," "Absolutes," etc., and these are the most expensive perfumery materials now available, the current price for violet being $1700 a pound.

Perfumers who use this class of material are apparently justified in the high price asked for their products.

The cost and variability, in both quality and price, of perfumery products from natural sources, has stimulated the modern organic chemist to search for synthetic perfume materials which would either replace or augment natural perfumes.

The painstaking efforts which have been made to determine the physical characteristics and chemical constituents of important volatile oils, that standards for pure products might be established, and the careful analysis of many other products, in pure research and for commercial purposes, has made available a vast amount of knowledge covering the constituents of these perfumes. With an exact record of the pure chemicals composing the perfume and the

proportion in which they exist in nature, the organic chemist theoretically is only required to prepare the various pure chemicals, mix them in the proportion indicated and produce artificially a rival of nature, which would always be uniform in quality and odor-value, and at a price subject to little fluctuation.

This dream of the synthetic chemist has today been partly realized. Many natural oils have been almost completely duplicated in the laboratory, and the chemist has also discovered chemicals which possess odors practically indentical with those in nature, but entirely unrelated chemically. Artificial musk admirably illustrates this fact.

The perfume chemist has also been able to reproduce many flower odors, which it has not been possible to extract from the flowers because of the minute quantity present; such odors as arbutus and sweet pea are illustrations.

It must not be thought, however, that synthetic perfumes always fully duplicate nature's odors. Often there are minute quantities of constituents which are so illusive that they escape the most careful analysis and others have defied reproduction, but sufficient has been done to fascinate and awe those who make a casual study of modern laboratory creation and to almost drive natural perfumery products from the field.

Taking up these synthetic and natural products side by side, it is possible to obtain interesting comparisons and also to note the available materials and the methods of production.

No strictly scientific odor classification has yet been made, since there seems to be no basis comparable to that of the spectrum for colors, but the following well-known perfume substances and odors have been arranged primarily from the standpoint of the chemical relation of the more important constituent. Grouped with these are all odors which resemble the key-odor but without regard to chemical affiliation, thus really making the classification one of related odors, alphabetically arranged.

The scope of this paper will not permit a complete listing of the constituents of every oil, only the more important having been included. Those who desire a more complete presentation of the chemistry of odorous substances are referred to Parry or Gildemeister and Hoffman.

Both the open and closed chain series of organic chemicals are represented among perfume products and a large variety of chemical structures, such as alcohols, ketones, aldehydes, esters, phenolic compounds, terpenes, etc., are found.

Nitrogen compounds are represented only in the musk-like products and sulphur must be rigidly excluded as even a minute trace will render most substances unfit for use.

ACACIA BLOSSOMS.

Yara.—The methyl ether of beta naphthol, commercially known as "Yara," is a very powerful odor used almost exclusively for perfuming soaps. One-quarter ounce will perfume 100 pounds of soap. This is an excellent illustration of the striking change in odor-value brought about by a slight modification of chemical structure. Betanaphthol, a medicinal chemical, not of itself a perfume, is changed by the introduction of the methyl group, CH_3, into a powerful perfume, not known to exist in nature.

ANISE OIL.

Anethol.—This definite chemical, a phenolic compound, is the chief constituent in the Oils of Anise and Star Anise.

ARBUTUS.

This odor, such a source of delight in the spring to those who have the time to search for the delicate blossoms hiding close to the ground, has been reproduced synthetically and is a grateful perfume.

BAY OIL.

This oil is not produced synthetically but one of its most important constituents is the definite chemical *Eugenol* found also in clove and other volatile oils.

This oil gives the distinctive odor to *"Bay Rum."*

BERGAMOT OIL.

Important pure chemical constituents of this citrus oil are:

Limonene, a terpene, also found in the oils of Lemon, Orange, Caraway, etc., also the alcohol *Linalol* $C_{10}H_{17}OH$, and

Linalyl Acetate, which is likewise found in lavender oil, and used in the artificial production of the oils of bergamot and lavender. Linalyl acetate also occurs in the oils of ylang ylang, petit grain, neroli, jasmine, gardenia, and others.

BITTER ALMOND OIL.

The natural oil largely consists of pure

Benzaldehyde, C_6H_5CHO, a chemical substance which may be produced synthetically.

Nitrobenzene, $C_6H_5NO_2$, *Oil of Mirbane.* It is not chemically identical with benzaldehyde but has an odor resembling Bitter Almond and is used as a cheap soap perfume.

CARNATION.

A substance known as

Iso-eugenol is found in small amounts in the oil of ylang ylang and nutmeg. It possesses a powerful carnation-like odor and is essential in the production of artificial carnation or *"œillet."*

Another modification of eugenol,

Methyl-eugenol, is found in the oils of calamus, cassie and bay. It possesses a distinct carnation-like odor and is used in manufacturing perfumes of the carnation type.

Caryophyllene, $C_{15}H_{24}$, obtained from the oils of cinnamon, clove and other oils, possesses an odor resembling carnation.

CASSIE OIL (resembling violets).

This oil from Acacia Farmesiana possesses an odor resembling the violet. It is obtainable, for perfumery, chiefly in the form of a pomade, although the oil is a commercial article.

It has been carefully analyzed and shown to contain the following definite chemical constituents:

Farnesol,
Geraniol,
Linlol,
Benzyl alcohol,

Methyl salicylate,
Adecylic aldehyde,
A carminic aldehyde,
An anisic aldehyde,
also a ketone of a violet-like odor.
A synthetic cassie is obtainable.

CINNAMON OIL.

In addition to

Cinnamic aldehyde, which is the most important constituent in the oils of cinnamon and cassia, there is found

Caryophyllene, a sesquiterpene, $C_{15}H_{24}$, having an odor resembling carnations.

CLOVE OIL.

The characteristic constituent in the oils of clove, cinnamon leaf, bay, and pimento is

Eugenol, $C_{10}H_{12}O_2$. This substance is chiefly important as the starting point for synthetic "vanillin."

GARDENIA.

Methyl Anthranilate, an ester, is one of the constituents of this oil and possesses the characteristic odor of the synthetic perfume resembling gardenia.

HAWTHORN.

Anisic Aldehyde—also known as "aubepine," is the basis for the above synthetic odor.

HELIOTROPE.

Heliotropin (*piperonal*). The methylene ether of protocatechuic aldehyde, a white crystalline substance, possesses a powerful odor resembling heliotrope and is the basis for synthetic heliotrope perfumes. It is an excellent blender and fixative.

HONEYSUCKLE.

The odor sold as *Honeysuckle* is prepared synthetically.

HYACINTH.

Phenyl Propyl Alcohol possesses a soft, heavy odor of the hyacinth type. The odor of *Cinnamic Alcohol* is also similar to hyacinth.

Another substance having a hyacinth-like odor is

Phenylacetic Aldehyde. It is not found naturally but is used in the synthetic production of a hyacinth odor.

Phenyl ether (Diphenyl Oxide) also resembles hyacinth and is much used in synthetic perfumery.

JASMINE OIL.

The analysis of natural jasmine oil, according to Hesse and Miller, shows about the following composition:

Benzyl Acetate	65.	parts
Linalyl	7.5	"
Benzyl alcohol	6.	"
Linalol	15.5	"
Indol	2.5	"
Jasmine (*a ketone*)	3.	"
Methyl anthranilate	0.5	"

Other entirely different chemical substances possess a jasmine-like odor, as

Brom-styrolene ($C_6H_5.CH.CHBr$)

Styrolene alcohol (or phenyl-glycol-methylene-acetol) $C_6H_5.CH(OH)CH_2OH$. Secondary styrolyl acetate $C_6H_5.CH(O.CO.CH_3)CH_3$ and are all used for making synthetic jasmine.

JONQUILLE.

This odor is obtainable from natural sources through the enfleurage process and is also made synthetically.

LABDANUM RESIN.

A ketone obtained from this resin,

Acetphenone, $C_6H_5.CO.CH_3$, is now made synthetically. It possesses a powerful odor and is used chiefly in soap perfumery.

LAVENDER FLOWER OIL.

The *alcohol Linalol,* $C_{10}H_{17}H$ and

Linalyl Acetate are important constituents of this oil and constitute the basis for the synthetic oil.

LEMON OIL.

This is a natural product, produced in enormous quantities in lemon-growing countries. It contains

Limonene, a terpene having the formula $C_{10}H_{16}$, which represents the largest proportion of the oil.

Linalol, an alcohol, $C_{10}H_{17}OH$, is also present and

Citral represents from 4 to 6 per cent. of the oil and gives it the characteristic flavor.

Citral is obtained artificially by oxidizing geraniol and is also extracted from lemon grass oil.

LILAC.

This odor is one of the triumphs of the synthetic chemist, as it is not obtainable from natural sources and is one of the most popular and pleasing of perfumes.

Terpineol, a terpene alcohol, $C_{10}H_{17}.OH$. It is the basis for most of the perfumes of the lilac type.

Various modifications are sold under the names *"Muguet," Syringol, lilacine* and *synthetic gardenia.* It is often blended with geranium oil, heliotropine, ylang ylang, sandalwood and rose. Heat, acid and alkali do not appreciably affect it.

LILY OF THE VALLEY.

This popular perfume is only obtainable synthetically and although it represents a compounded product the basis is the alcohol terpineol.

MAGNOLIA.

This is again a purely synthetic perfume.

Ethyl acetate $C_2H5.C_2H_3O_2$ is found in small amounts in the natural magnolia.

MEADOW SWEET.

Salicylic aldehyde is said to be the basis for this perfume.

NARCISSUS.

Phenylacetic aldehyde is said to be the basis for the synthetic narcissus perfumes.

NEROLI OIL (ORANGE FLOWERS.)

The odor of orange flowers has long been highly prized as a perfume. The unmodified odor of the flowers is obtainable from pomades, concretes, absolutes and from Orange Flower Water. The distilled oil known as Oil of Neroli, possesses a valuable but distinctly altered odor. This oil is the most pronounced odor in "Cologne Water" which has been a popular perfume for more than a hundred years.

Synthetic Neroli is also obtainable and the oil has been shown to contain the following pure chemicals and possibly others:

Indol, C_8H_7N, found in the oils of orange and jasmine flowers.

Phenyl-ethyl alcohol $C_6H_5CH_2.CH_2OH$

Methyl Anthranilate—The methyl ester of ortho-amido—benzoic acid.

Ethyl Anthranilate—Sweeter and better than the methyl ester.

Octyl Aldehyde—$CH_3(CH_2)_6CHO$—A natural constituent.

Other substances have been found to resemble the odor of orange flowers and are much used in synthetic perfumery.

Phenyl ether (Diphenyl oxide) is one of these.

Bromelia—The ethyl ether of beta-naphthol, is a powerful odor resembling orange flowers and used in perfuming soap. One-quarter ounce will perfume 100 pounds of soap.

NEW MOWN HAY.

The basis of this long popular perfume is a delightfully odorous substance found naturally in the tonka bean, in newly cut grass, and also made synthetically.

It serves also as a fixative.

ORANGE OIL.

This valuable oil is obtained from the natural source, the rind of the orange.

Limonene a terpene $C_{10}H_{16}$ constitutes the larger part of the oil.

ORCHIDS.

The perfume sold under this title is purely synthetic and

Amyl Salicylate is the base usually employed. Perfumes on the "Orchid" type are also sold as *"orchidae," trefle,* or *trefoil,* etc.

ORRIS.

"Orris Root" as it is commercially known, the rhizome of *Iris florentina,* possesses a pleasing odor resembling violets, and was for many years the most important artificial violet odor.

Ground or powdered Orris is today the basis for most sachets. The oil and the ketone *irone,* obtained from the oil and also produced synthetically, being isomeric with ionone, is yet an important factor in producing modern violet perfumes.

PALMAROSA OIL.

Geraniol, $C_{10}H_{17}OH$, also an important constituent in Oil of Rose is found in this oil.

PINE OIL.

This pleasantly smelling oil, suggesting the pine forests, is used in the industries and in medicine and has also found a place in perfumes of the type used for refreshing the air of rooms where cheapness and refreshing effects are essential.

Some of its chemical constituents are:

Pinene, Camphene and *Sylvestrene,* terpenes having the formula $C_{10}H_{16}$.

Sylvestrene is also found in terpentine.

PINE NEEDLE OIL.

This oil is very similar to Pine Oil.

Bornyl Acetate is an important constituent.

ROSE.

Rose, for centuries, has been one of the most valued perfumes and fortunately the natural course has provided materials for the perfumer. Rose petals, carefully dried, and preserved in an ornamental jar is the chief odorous substance used in the perfume

known as *"potpourri."* The oil has long been distilled and is usually known as *"Otto of Rose."* The distilling of Rose Oil in Bulgaria, from where the largest amount has long been obtained, is today a government monopoly. The roses are grown for the oil and an acre yields about 100 pounds of roses each day for about three weeks.

In Southern France the roses are grown primarily for the flower market but much Oil of Rose is distilled.

In Bulgaria it is said that it requires about 3000 pounds of roses to produce one pound of oil. In France from 10,000 to 20,000 pounds of roses to produce one pound of oil.

The natural rose perfume is also available from pomads and as Rose Water. The Oil of Rose has been carefully analyzed and shown to consist of solid stearoptenes, representing about 33 per cent. of the oil, complex alcohols, about 50 per cent. and esters. A typical analysis is as follows:

Stearoptenes (paraffin hydrocarbons, $C_{16}H_{34}$)	33.5 parts
Geranyl acetate,	1.6 parts.
Geranyl Phenylacetate Citronellol, $C_{10}H_{19}OH$ Geraniol, $C_{10}H_{17}OH$ Rhodinol, $C_{10}H_{19}OH$ Phenyl ethyl alcohol, $C_6H_5.CH_2.CH_2OH$ Nerol Fornesol Ethylic alcohol Linalol, $C_{10}H_{17}OH$	All alcohols 50.0 parts

These definite chemicals have all been made synthetically or separated from other oils and enter into synthetic Rose products.

Other chemical substances possess roselike odors and are used in preparing synthetic Oil of Rose. Some of these are:

Octyl Alcohol
Octyl aldehydc
Citronellyl Acetate
Phenyl-ethyl Propionate
Geranyl Butyrate used chiefly for perfuming soaps.

ROSE GERANIUM OIL.

This oil consists chiefly of geraniol, 27 to 58 per cent., Citronellol, 42 to 73 per cent. Also Linalol.

The larger the proportion of Citronellol, the better the grade.

The following additional chemical substances are of interest in connection with Geranium Oil:

Geranyl formate is not found naturally in the oil, but has a sweet, rose-geranium-like odor.

Citronellyl Acetate is used in blending the synthetic oil.

The basis of most synthetic Geranium Oils is

Phenyl ether (Diphenyl oxide), $C_6H_5.O.C_6H_5$.

ROSEMARY OIL.

One of the constituents of this oil is

Bornyl Acetate.

SANTALWOOD OIL.

This oil, used in small amounts, chiefly as a fixative, contains *Santalene*, a sesqueterpene, $C_{15}H_{24}$, and

Santalol, an alcohol, $C_{15}H_{24}O$.

SWEET PEA.

This delicate odor has been admirably reproduced synthetically.

TUBEROSE.

The odor of the tuberose does not pre-exist in the plant as a volatile oil, but is the result of chemical action upon constituents, among which are Benzyl Alcohol and Menthyl Anthranilate.

VANILLA.

Vanilla is usually thought of as a flavoring substance, but the crystallizable aldehyde, vanillin, present in the beans, possesses odor value and excellent fixative qualities.

Vanillin ($C_8H_8O_3$) methyl protocatechuic aldehyde, besides occurring naturally in the vanilla bean (about 2 per cent.) is also found in benzoin and the balsams of Peru and Tolu. The commercial product, however, is prepared artificially by various processes, the most important being the oxidation of eugenol from oil of clove.

VERBENA OIL.

This oil has been used as a cheap form of perfume.

VERTIVERT.

Both the oil and the ground root have been used in perfumery.

VIOLET.

The violet perfume is the most popular of odors, but Violet flowers contain so small an amount of volatile oil that when obtained from natural sources it becomes the most expensive perfume material known. According to Isokovics one pound of fresh flowers cost in the producing districts of France from 25 to 35 cents and four pounds of flowers yield only one grain of oil when all non-odorous constituents are excluded. This would make the true flower oil cost over $7000 a pound and it is interesting to note that in a current price list, a concentrated extract of violet flowers is quoted at $1700 per pound. It can therefore be seen that the discovery of a synthetic product possessing the true violet odor was a valuable contribution to perfumers' art.

This substance is known as Ionone and a number of modifications have been developed.

Ionone. From the standpoint of modern perfumery, this ketone is considered essential for the production of violet odors.

It is now marked in two forms known as Alpha-ionone and Beta-ionone. *A-ionone* is said to have a sweeter and more penetrating odor, rather resembling orris, while the *b-ionone* is more like the true violet flowers. They are very powerful and must be largely diluted, at least one to one thousand and blended with other substances to produce the desired effect.

Irone. A ketone naturally present in Orris Oil, is isomeric with ionine and has the formula $C_{13}H_{20}O$. It possesses an odor resembling violet and is used in violet perfumes.

WINTERGREEN OIL.

This oil, chiefly used as a flavor, contains about 99 per cent. of *Methyl Salicylate,* a definite chemical, $CH_3C_7H_5O_3$. The *Oils of Betula and Sweet Birch* contain about the same amount of methyl salicylate and the Pharmacopœia considers the three products identical from the therapeutic standpoint.

Methyl Salicylate is prepared synthetically on a large scale.

YLANG YLANG OIL.

This oil is largely obtained from the Philippine Islands, Java, and Southern Asia, and the name means "flower of flowers."

It possesses perfume value and analysis shows it to contain

Linalol,
Geraniol,
Codinene,
Methyl ether of eugenol,
" " " iso-eugenol,
Methyl benzoate
" salicylate,
Benzyl acetate
" benzoate,
" alcohol, and
Methyl anthranilate.
It is prepared synthetically.

"ORIENTAL ODORS."

A type of odor which is intense, heavy, and lingering, containing such substances as santalol, cedrol, patchouli alcohol, guaiol, is referred to as an oriental odor. Another name applied to this class of odors is "Trefle." These odors are all compounded and do not represent any natural flower. A number of samples are displayed, which represent this class.

COMPOUNDED ODORS.

In addition to the well-known flower odors as rose, lilac, violet, etc., the perfumer has developed blends of odorous substances to which a fanciful name is attached.

This tendency has been very marked of recent years and special names like "Djer-Kiss," "Ideal," "Adoration," "Azurea," "Mary Garden," etc., are being controlled and extensively advertised.

The possibility for new odors in this class of perfumes is unlimited with the hundreds of natural and synthetic odors made available for the perfumer.

Samples of some of these are shown.

FIXATIVES.

As already mentioned, the perfumer has found it necessary to add to perfumes certain substances which lessen the volatility of the floral odors and increase the permanency of the product. These substances in themselves often possess a disagreeable odor, but are used in small amounts and are unnoticed in the finished perfume.

Some of the substances of this character are of animal origin, as musk, civet, castor and ambergris, others are from vegetable sources, as gum-resins and balsams, while still others are synthetic, as heliotropin, vanillin, coumarin, synthetic musk, civet, etc.

Musk. Natural Musk is a dried secretion obtained from the Musk deer. It is excessively costly and difficult to procure in pure form as the animal from which it is obtained frequents the mountain heights of interior Asia, chiefly Thibet, and is almost extinct because of the many years that it has been hunted. Today it is quoted at from $50 to $80 an ounce and recent purchases of the tincture cost $9 for four fluid ounces.

Fortunately the odor and fixative value, which apparently is due to a ketone, has been largely duplicated by the chemist but by an entirely different chemical entity.

Artificial Musk. The true Musk ketone is without the presence of nitrogen, but several nitrogenous compounds have been produced which strongly resemble the musk odor.

The chemical constituents of some of the artificial musks are as follows:

Tri-nitro-butyl xylene (*"xylene musk"* or *"Musk-Baur"*).
Butyl-xylene-propyl ketone (*"ketone musk"*).
Dinitro-tertiary-butyl-xylene-aldehyde (*"aldehydemusk"*).
Dinitro-tertiary-butyl-xylene-cyanide (*"cyanide musk"*).
Musk Ambrette or *Dinitro-butyl-meta-cresol-methyl ether* is also a substance having a musk-like odor.

Ambergris—The substance which has long been prized as a fixative is an animal decomposition product ejected by the Sperm Whale and usually found floating on the ocean. The better qualities are worth at least $25 an ounce.

A practically identical synthetic product has been produced which can be sold for $50 a pound.

Civet—A secretion obtained from the civet cat, is valuable as a fixative. The natural product is obtainable at a reasonable price, as the animal from which it is procured is domesticated in the East Indies and the secretion may be secured by scraping the secretion gland.

Synthetic Civet is also available and is sold under the name of "Civettine."

Castor—A secretion product resembling civet, obtained from the beaver. This product was at one time extensively used in the practice of medicine but has fallen into disuse.

Storax, a balsam for many years obtained from the oriental sweet-gum (Liquidambar orientalis) but now also commercially available from the "sweet-gum" tree of America (Liquid-ambar styraciflua) is used as a fixative in perfumery. That portion of Storax which gives it value in perfumery consists of the cinnamic acid esters of ethyl, benzyl, phenyl, propyl and cinnamyl alcohols also phenyl propyl alcohol, cinnamyl alcohol and vanillin.

Balsam of Peru consists chiefly of benzyl cinnamate and benzoate, free benzoic and cinnamic acids. An alcohol named peruviol and small amounts of fornesol, cinnamic alcohol and vanillin.

Balsam of Tolu consists chiefly of a terpene, phellandrene, benzyl benzoate, benzyl cinnamate and fornesol.

Amyl Benzoate and *Benzyl Benzoate* are among the best known fixatives and the latter is also used in perfumery as a solvent for artificial musk, the so-called *"musk oil"* being a solution of artificial musk in benzyl benzoate.

Heliotropin, vanillin and *coumerin* all possess valuable fixative as well as perfume qualities. These have all been referred to elsewhere in this paper and details given.

Fruit Flavors.

Many artificial fruit flavors have been marketed having odors and flavors similar to those of the natural fruit. To most people, however, the results have been disappointing. It is interesting to note that at the present time Dr. Frederick W. Power, a research chemist of international reputation is engaged in the U. S. Bureau of Chemistry, upon a study of the composition of important fruit flavors.

The results of this work is being published in a series of Government Bulletins and this investigation has already made it possible to greatly improve some artificial fruit flavors and promises gratifying and valuable results.

In preparing this review of the perfumery industry, the following books have been consulted:

"Chemistry of Essential Oils and Artificial Perfumes" (Parry).
"Volatile Oils" (Gildemeister and Hoffman).
"Cosmetics" (Koller).
"The Art of Perfumery" (Piesse).
"Synthetic Perfumes and Flowers" (Isakovics).

STUDIES IN EXTRACTION.

II. The Rate of Extraction of Cascara Sagrada.

By James F. Couch.

In an earlier paper[1] I described the procedure and reported the results obtained in a determination of the rate at which Phytolacca decandra is extracted with the menstruum (diluted alcohol) used in the process of the U. S. P. 8. Following that investigation a sample of cascara sagrada was extracted, the percolate was collected in fractions and these were analyzed for alcohol content and extract, and the specific gravity was determined.

Certain innovations were introduced into the general procedure which made it somewhat different from that followed in the case of Phytolacca, chief of which were: The menstruum (40 per cent. alcohol by volume) was all mixed at one time instead of in five-gallon lots as was done with the Phytolacca. This procedure ensured a non-varying menstruum which the former method did not. This detail was important because it was intended that a careful study of the changes in alcoholic content of the percolate should be made and possible error due to slight differences in the menstruum was thereby avoided. Another innovation was the change in the collection of the fractions. In the former experiment the percolate was collected in equal fractions of one gallon each until the drug was exhausted; in this study the first five gallons of percolate were collected in one-gallon lots, the next ten gallons were collected in two-gallon lots making five samples in all, and the remaining twenty gallons of

[1] This Journal, Vol. 93, pp. 419-26 (1921).

percolate which were collected were taken in lots of five gallons each, or four samples. The total number of samples of percolate was, therefore, fourteen.

Mathematical treatment of the data obtained from these samples similar in nature to that applied to the data from Phytolacca yielded the same sort of results. There was the same progressive variation, either a numerical increase or a decrease, and no constant was obtained. The unknown factors which operated with Phytolacca evidently played a rôle in the extraction of this cascara.

The results obtained (see Table I) agree with those from Phytolacca which indicates that the general course of extraction is qualitatively the same in both drugs. There is the same rapid initial extraction, the regularity, and the retardation. When fifteen gallons of percolate had been collected, that is when 300 ml. of menstruum for each 100 gm. of drug had percolated through, the quantity of extract removed was 95.34 per cent. of the total extract obtained. The cascara yielded 31.93 per cent. of extract or slightly less than the Phytolacca (32.75 per cent.), and, with the latter drug, an equivalent quantity of menstruum removed 97 per cent. of the total extract. Consequently the cascara is a trifle more difficult to extract.

The alcoholic content of each of the samples was determined and the results were very interesting. The minimum amount occurred in the first sample which contained 33.78 per cent. The increase in alcoholic content was slow and did not reach the maximum until the ninth sample. Thenceforward the alcoholic content of the percolate was essentially constant. It may be noted here that this change in content of alcohol is not due solely to the decrease in quantity of extract, but is also due to variation in the alcoholic content of the solvent inasmuch as the first portions of percolate contain the drug moisture which dilutes the menstruum.

Another interesting result was the extract content of sample 2 which was larger than that of sample 1. This recalls the similar case described by Lloyd.[2] It may be explained by the assumption[3] that during the maceration a part of the first fraction has saturated the cotton or excelsior at the bottom of the percolator and so has been quite out of contact with the drug.

[2] This Journal, Vol. 50, p. 438 (1878).
[3] This Journal, Vol. 92, p. 792 (1920).

EXPERIMENTAL.

A quantity of cascara was purchased on the open market, identified, and ground to a coarse powder. 18.9 kg. of this drug were percolated according to the directions in the U. S. P. 8 for fluid-extract of cascara. The drug was thoroughly moistened with the menstruum in a mechanical mixer and the whole was packed firmly and evenly in a galvanized iron percolator of about twenty-five gallons capacity. The percolator was set in place and enough menstruum was added to the drug to saturate it and leave a stratum above. When a few drops of percolate appeared at the lower orifice the outlet was closed, the percolator was tightly covered and the drug was allowed to macerate for exactly forty-eight hours. Percolation was then commenced and the rate of flow of percolate was adjusted so that one gallon was obtained in about one and one-half hours. The percolation was discontinued at 5.30 P. M. each day and was recommenced at 8 A. M. the following morning; the date of starting was so chosen that a Sunday did not occur to interrupt the percolation.

The fractions of percolate were collected in clean bottles connected by a rubber tube with the percolator. The whole fraction was thoroughly mixed and a sample was taken for analysis.

The extreme variations of temperature during the process were 21° C. and 27° C.

Fresh menstruum was added to the percolator continually to replace that percolated out so that the stratum above the drug was fairly constant.

The specific gravity, alcohol and extract content of the samples was determined by the methods adopted in the study on Phytolacca.

The data obtained is recorded in Table I.

TABLE I.

Sample No.	Quantity Gals.	Extract per 100 ml. Gm.	Corrected Extract Gm.	S. G. of Percolate.	Abs. Alc. by Vol.	% of Total Extract.
1	1	19.470	19.470	1.0190	33.78	12.18
2	1	19.684	19.684	1.0180	33.94	12.32
3	1	18.116	18.116	1.0150	34.30	11.34
4	1	16.816	16.816	1.009	34.64	10.77
5	1	15.504	15.504	1.004	35.16	9.704
6	2	12.304	24.608	0.9970	35.80	15.40

Sample No.	Quantity Gals.	Extract per 100 ml. Gm.	Corrected Extract Gm.	S. G. of Percolate.	Abs. Alc. by Vol.	% of Total Extract.
7	2	8.848	17.696	0.9837	36.90	11.08
8	2	5.456	10.912	0.9736	38.76	6.83
9	2	3.120	6.240	0.9653	39.76	3.906
10	2	1.640	3.280	0.9599	39.76	2.053
11	5	0.700	3.500	0.9556	39.80	2.191
12	5	0.376	1.880	0.9542	39.76	1.177
13	5	0.236	1.180	0.9537	39.72	0.738
14	5	0.176	0.880	0.9529	39.72	0.550

SUMMARY.

1. The extraction of the official bark of cascara sagrada proceeds regularly with diminishing velocity.

2. The factors which determine the rate of extraction are those found in the study of Phytolacca.

3. A quantity of percolate equivalent to 300 ml. per 100 gm. of drug extracted 95 per cent. of the total extract. Cascara is somewhat more difficult to extract than is Phytolacca.

4. The change in alcoholic content of the percolate was studied quantitatively and the results are reported.

ABSTRACTED AND REPRINTED ARTICLES

PHARMACEUTICAL ETHICS.*†

A Historical Review of the Subject With Examples of Codes Adopted or Suggested at Different Periods, Together With a Suggested Code for Adoption by Present-Day Associations.

By Charles H. Lawall.[1]

Ethics is the science of human duty. A code of ethics is a carefully formulated system of principles or rules of practice for the guidance of a particular group of individuals, such as the members of a profession.

The Mosaic law is a code of ethics in the broadest sense as applied to humanity at large.

The development of codes of ethics is an indication of the evolution and growth of moral consciousness. Ethics and morality are not always synonymous; neither are ethics and legality. "Right" and "wrong" are terms which have different meanings and interpretations at different periods.

The necessity for specific principles for the guidance of individuals having common interests, in addition to the tenets of religion and morality, has been recognized from the earliest historical periods. Probably the most ancient code of professional ethics is the Hippocratic Oath, which has been in existence for about 2500 years, and which is an eminently suitable starting point for a discussion of the subject. One of the several translations is as follows:

"THE HIPPOCRATIC OATH.

"I swear by Apollo the physician, and Aesculapius, and Hygeia, and Panacea, and all the gods and all the goddesses—and I make them my judges—that this mine oath and this my written engagement I will fulfil as far as power and discernment shall be mine.

*Presented before Section on Education and Legislation, A. Ph. A., New Orleans meeting, 1921.

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[1] Dean of the Philadelphia College of Pharmacy and Science.

"Him who taught me this art I will esteem even as I do my parents; he shall partake of my livelihood, and, if in want, shall share my goods. I will regard his issue as my brothers and will teach them this art without fee or written engagement if they shall wish to learn it.

"I will give instruction by precept, by discourse, and in all other ways to my own sons, to those of him who taught me, to disciples bound by written engagements and sworn according to medical law, and to no other person. So far as power and discernment shall be mine, I will carry out regimen for the benefit of the sick and will keep them from harm and wrong. To none will I give a deadly drug, even if solicited, nor offer counsel to such an end; likewise to no woman will I give a destructive suppository; but guiltless and hallowed will I keep my life and mine art. I will cut no one whatever for the stone, but will give way to those who work at this practice.

"Into whatsoever houses I shall enter I shall go for the benefit of the sick, holding aloof from all voluntary wrong and corruption, including venereal acts upon the bodies of females and males, whether free or slaves. Whatsoever in my practice or not in my practice I shall see or hear amid the lives of men which ought not to be noised abroad—as to this I will keep silence, holding such things unfitting to be spoken.

"And now if I shall fulfil this oath and break it not, may the fruits of life and art be mine, may I be honored of all men for all time; the opposite if I shall transgress or be forsworn."

The foregoing is a splendid example of exalted idealism, couched in virile, dignified language, and applicable to present day conditions, with minor changes.

In the twelfth century A. D. there lived a Jewish physician and teacher named Maimonides, who is ranked by medical historians as the greatest Jew after Moses. He was born at Cordova, Spain, then under Arabic domination, and his Arabic name was "Abu Amran Musa Ben Maimum Obaid Alla el Cordovi."

He contributed the next great landmark in the literature of professional ethics in the shape of a combined oath and invocation.

"THE OATH AND PRAYER OF MAIMONIDES.

"Thy Eternal Providence has appointed me to watch over the life and health of Thy creatures. May the love for my art actuate me at all times; may neither avarice, nor miserliness, nor the thirst

for glory, or for a great reputation engage my mind; for the enemies of Truth and Philanthropy could easily deceive me and make me forgetful of my lofty aim of doing good to Thy children.

"May I never see in the patient anything but a fellow creature in pain.

"Grant me strength, time and opportunity always to correct what I have acquired, always to extend its domain; for knowledge is immense and the spirit of man can extend infinitely to enrich itself daily with new requirements. Today he can discover his errors of yesterday and tomorrow he may obtain a new light on what he thinks himself sure of today.

"O God, Thou hast appointed me to watch over the life and death of Thy creatures; here am I ready for my vocation.

"And now I turn unto my calling:

O stand by me, my God, in this truly important task;
Grant me success! For—
Without Thy loving counsel and support,
Man can avail but naught.
Inspire me with true love for this my art
And for Thy creatures,
O, grant—
That neither greed for gain, nor thirst for fame, nor vain ambition,
May interfere with my activity.
For these I know are enemies of Truth and Love of men.
And might beguile one in profession,
From furthering the welfare of Thy creatures.
O strengthen me.
Grant energy unto both body and the soul
That I might e'er unhindered ready be
To mitigate the woes,
Sustain and help
The rich and poor, the good and bad, enemy and friend,
O let me e'er behold in the afflcted and the suffering,
Only the human being."

Both of these refer particularly to medical practice. The earliest rules for guidance of pharmacists which I have been able to find, occur in the sixteenth century. Bulleyn, a cousin of Queen Anne Bulleyn and a prominent English apothecary of that century, is authority for the following rules for the guidance of the apothecaries of his day.

"The apothecary must first serve God; forsee the end, be cleanly and pity the poor. His place of dwelling and shop must be cleanly to please the senses withall. His garden must be at hand with plenty of herbs, seeds and roots. He must read Dioscorides. He must have his mortars, stills, pots, filters, glasses, boxes, clean and sweet. He must have two places in his shop, one most clean for physic, and the base place for chirurgic stuff. He is neither to increase nor diminish the physician's prescription. He is neither to buy nor sell rotten drugs. He must be able to open well a vein, for to help pleurisy. He is to meddle only in his own vocation, and to remember that his office is only to be the physician's cook."

Some of these rules are still worthy of consideration in a modern code of ethics. It is particularly interesting to note, however, the viepwoint of that day as regards the relative importance of medicine and surgery, for in a modern store, the "chirurgic stuff" is given the cleanest place and not the one which is "base."

The seventeenth century saw the famous battle between the Galenists and the Paracelsists, and the development of guilds and societies of apothecaries, whose records are not easily accessible or widely copied. One item of collateral interest from this period is the oath of the journeymen apothecary of Germany, which is referred to as follows:

"Every journeyman apothecary shall take an oath that he will faithfully serve, not only his master, but also the members of the community at large. That he will prepare all medicines 'secundum artem,' and of pure drugs, whether they be such as are annually examined by the authorities or not. That he will dispense no poison, opiate or emmenagogue without the knowledge of the master, or endanger the life of any one by his carelessness. That he will not deliberately change a physician's prescription, and will abstain from excessive indulgence in intoxicating drinks and will at all times set a good example to the apprentice. That he will not leave the shop without the knowledge of the master, and particularly not absent himself at night. That he will be devoted to his master, to the *visitatori medico,* and to each of the doctors of the incorporated Collegio Medico. He shall swear that he will do all this according to his best ability."

The eighteenth century saw the rise of proprietary medicines and some of our well-known and respectable preparations of the pres-

ent pharmacopœias of the world originated as secret formulas or prescriptions of eminent physicians during this period, in which little of constructive value to the ethics of the calling seems to have come down to us.

In the early part of the nineteenth century, pharmaceutical education in America had its beginning in the founding of the Philadelphia College of Pharmacy in 1821.

The first code of ethics of this organization, which is the earliest code of pharmaceutical ethics that has a direct connection with and applicability to present day practice, was adopted in 1848, and reads as follows:

"A CODE OF ETHICS ADOPTED BY THE PHILADELPHIA COLLEGE OF PHARMACY.

"Pharmacy being a profession which demands knowledge, skill, and integrity on the part of those engaged in it, and being associated with the medical profession in the responsible duties of preserving the public health, and dispensing the useful though often dangerous agents adapted to the cure of disease, its members should be united on some general principles to be observed in their several relations to each other, to the medical profession, and to the public.

"The Philadelphia College of Pharmacy being a permanent, incorporated institution, embracing amongst its members a large number of respectable and well educated apothecaries, has erected a standard of scientific attainments, which there is a growing disposition on the part of candidates for the profession to reach; and being desirous that in relation to professional conduct and probity, there should be a corresponding disposition to advance, its members having agreed upon the following principles for the government of their conduct:

"1st. The College of Physicians of Philadelphia having declared that any connection with, or monied interest in apothecaries' stores, on the part of the physicians, should be discountenanced; we in like manner consider that an apothecary being engaged in furthering the interests of any particular physician, to the prejudice of other reputable members of the medical profession, or allowing any physician a percentage or commission on his prescriptions, as unjust toward that profession and injurious to the public.

"2nd. As the diagnosis and treatment of disease belong to the province of a distinct profession, and as a pharmaceutical education does not qualify the graduate for these responsible offices; we should, where it is practicable, refer applicants for medical aid to a regular physician.

"3d. As the practice of Pharmacy can only become uniform, by an open and candid intercourse being kept up between apothecaries, which will lead them to discountenance the use of secret formulæ, and promote the general use and knowledge of good practice, and as this College considers that any discovery which is useful in alleviating human suffering, or in restoring the diseased to health, should be made public for the good of humanity and the general advancement of the healing art—no member of this College should originate or prepare a medicine, the composition of which is concealed from other members, or from regular physicians.

"Whilst the College does not at present feel authorized to require its members to abandon the sale of secret or quack medicine, they earnestly recommend the propriety of discouraging their employment, when called upon for an opinion as to their merits.

"4th. The apothecary should be remunerated by the public for his knowledge and skill, and his charges should be regulated by the time consumed in preparation, as well as by the value of the article sold; although location and other circumstances necessarily affect the rate of charges at different establishmnts, no apothecary should intentionally undersell his neighbors with a view to his injury.

"5th. As medical men occasionally commit errors in the phraseology of their prescriptions, which may or may not involve ill consequences to the patient if dispensed, and be injurious to the character of the practitioner; it is held to be the duty of the apothecary, in such cases, to have the corrections made, if possible, without the knowledge of the patient, so that the physician may be screened from censure. When the errors are of such a character as not to be apparent, without the knowledge of circumstances beyond the reach of the apothecary, we hold him to be blameless in case of ill consequences, the prescription being his guarantee, the original of which should always be retained by the apothecary.

"6th. Apothecaries are likewise liable to commit errors in compounding prescriptions—first, from the imperfect handwriting of the

physicians; secondly, owing to the various synonyms of drugs in use, and their imperfect abbreviations; thirdly, from the confusion which even in the best regulated establishments, may sometimes occur, arising from press of business; and fourthly, from deficient knowledge or ability of one or more of the assistants in the shop, or of the proprietor—

"We hold that in the first three instances named, it is the duty of the physician to stand between the apothecary and the patient, as far as possible; and in the last that he should be governed by the circumstances of the case—drawing a distinction between an error made by a younger assistant accidentally engaged, and a case of culpable ignorance or carelessness in the superior.

"7th. As the apothecary should be able to distinguish between good and bag drugs, in most cases, and as the substitution of a weak or inert drug for an active one, may, negatively, be productive of serious consequences—we hold that the intentional sale of impure drugs or medicines, from motives of competition, or desire of gain, when pure articles of the same kind may be obtained, is highly culpable, and that it is the duty of every honest apothecary or druggist to expose all such fraudulent acts as may come to his knowledge. But in reference to those drugs which cannot be obtained in a state of purity, he should, as occasion offers, keep physicians informed as to their quality, that they may be governed accordingly.

"8th. As there are many powerful substances that rank as poisons, which are constantly kept by apothecaries, and prescribed by physicians, and which are only safe in their hands, as arsenious acid, vegetable alkaloids, ergot, cantharides, etc.—we hold that the apothecary is not justified in vending these powerful agents indiscriminately to persons unqualified to administer them, and that a prescription should always be required, except in those cases when the poisons are intended for the destruction of animals or vermin—and in these instances only with the guarantee of a responsible person. And we hold that when there is good reason to believe that the purchaser is habitually using opiates or stimulants to excess, every conscientious apothecary should discourage such practice.

"9th. No apprentice to the business of apothecary should be taken for a less term than four years, unless he has already served a portion of that time in an establishment of good character. Ap-

prentices should invariably be entered as matriculants in the school of pharmacy and commence attendance on its lectures at least two years before the expiration of their term of apprenticeship; and as the progress of our profession in the scale of scientific attainment must depend mainly upon those who are yet to enter it—it is recommended that those applicants who have had the advantage of a good preliminary education, including the Latin language, should be preferred.

DANIEL B. SMITH, *President.*
CHARLES ELLIS, *1st Vice-President.*
SAMUEL F. TROTH, *2nd Vice-President.*

Attest: DILLWYN PARRISH, *Secretary.*"

If the Quaker apothecaries had done nothing else of moment this code would remain as a monument to the lofty principles which actuated these men who were not simply theorists, but who carried into their daily work the idealism which they held up as a pattern to their professional brethren.

In 1900 this code of ethics was somewhat modified and it now has the following form:

"THE PHILADELPHIA COLLEGE OF PHARMACY REVISED CODE OF ETHICS.
(Adopted December 31, 1900.)

"The Pharmaceutical profession being one which demands knowledge, skill and integrity on the part of those engaged in it, and being associated with the medical profession in the responsible duties of preserving the public health and dispensing the useful though often dangerous agents adapted to the cure of disease, its members should be united on the ethical principles to be observed in their relations to each other, to the medical profession and to the public.

"*The Philadelphia College of Pharmacy* being an incorporated institution, embracing among its members a large number of eminent pharmacists, manufacturers, chemists and scientists, has erected and consistently maintained a high standard of scientific attainment, which there is a growing disposition on the part of candidates for the profession to reach; and being desirous that, in relation to professional conduct and probity, there shall be a corresponding disposition to advance, its members have subscribed to the following

fundamental principles for the government of their professional conduct.

"1st. We accept the *United States Pharmacopœia* as our standard and guide for all official preparations.

"In compounding a prescription written in a foreign country the *Pharmacopœia* recognized as authority in that country is to be followed. For unofficial preparations we advocate the adoption of uniform formulas in accordance with the *National Formulary* or other standard works, published by national or international agreement.

"2d. The practice of Pharmacy can become uniform only by an open and candid intercourse between apothecaries, which will lead them to discountenance the use of secret formulas in dispensing, and promote the general use and knowledge of improved methods. This College considers that any discovery which is useful in alleviating human suffering or in restoring the diseased to health, should be made public for the good of humanity and the general advancement of the healing art. We particularly deprecate the use of secret formulas between physician and pharmacist.

"While, at present, the College does not feel authorized in requiring its members to abandon the sale of proprietary medicines, it earnestly recommends the propriety of discouraging their employment.

"3d. The apothecary should be remunerated by the public for knowledge and skill, and the charges should be regulated by the time consumed in preparation, as well as by the cost of the article sold. Although location and other circumstances necessarily affect the rate of charges at different establishments, no apothecary should intentionally undersell his neighbors with a view to their injury.

"4th. No apothecary should be engaged in furthering the interests of any particular physician to the prejudice of other reputable members of the medical profession. We emphatically condemn the allowance of any percentage on prescriptions to physicians as unjust to the public and detrimental to both professions.

"5th. As the diagnosis and treatment of disease belong to the province of medicine, and as a pharmaceutical education does not qualify the pharmacist for the discharge of these responsible duties, we should, where it is practicable, refer applicants for medical aid

to a regular physician. And we likewise hold that medical practitioners should recognize the value of pharmaceutical education and relegate the compounding of prescriptions and the dispensing of all medicines to pharmacists.

"6th. As medical practitioners occasionally commit errors in their prescriptions, which may or may not involve ill consequences to the patient if dispensed, and be injurious to the character of the prescriber, it is held to be the duty of the apothecary in all such cases to protect the physician and to have the corrections made, if possible, without the knowledge of the patient, so that the physician may be screened from censure. When the errors are of such a character as not to be apparent, without the knowledge of circumstances beyond the reach of the apothecary, we hold him to be blameless in case of ill consequences. As the original prescription is his guarantee, we recommend that it should always be retained by the apothecary.

"Apothecaries, likewise, are liable to commit errors in compounding prescriptions, and we hold that in all such cases it is the duty of the physician to protect the interests of the dispenser and stand between him and the patient as far as possible.

"7th. The apothecary should be able to distinguish between good and bad drugs, and as the substitution of a weak or inert drug for an active remedy may be productive of serious consequences, duty demands that he should exercise his expert knowledge and good judgment in the selection and preparation of all remedies. We hold that substitution or the sale of impure drugs or medicines, when pure articles can be obtained, is highly culpable, and that it is the duty of every apothecary or druggist to expose all such fraudulent acts as may come to his knowledge.

"8th. As there are many powerful substances that rank as poisons, which are constantly kept by apothecaries and prescribed by physicians, and which are only safe in their hands, we hold that the apothecary is not justified in vending these powerful agents indiscriminately to persons unqualified to administer them, and that a prescription should always be required when intended for medicinal use. When the poisons are intended for technical purposes, or for the destruction of animals or vermin, the sales should only be made to responsible persons and strictly in accordance with the State law governing the sale of such poisons.

"9th. While we recognize the value of spirituous liquors as therapeutic agents and the necessity for pharmacists dispensing these legitimately in accordance with the physicians' prescriptions, we condemn as degrading and unprofessional any attempt to make such sales a prominent feature of the business.

"We discountenance any attempt to foster or increase the use of opiates or injurious drugs possessing the power of enslaving the consumer to habitual use.

"We hold that where there is good reason to believe that the purchaser is habitually using stimulants, opiates or other injurious drugs, we should discourage such practice by every means possible, and we urge upon pharmacists the duty of exercising at all times a conscientious care in dispensing drugs liable to such dangerous abuse.

"10th. As Pharmacy is a progressive profession, its followers should, by continuous study and application, keep abreast of the advances made in medicine and the sciences. It becomes our duty to encourage the elevation of our chosen profession by stimulating research, investigation and study.

"Special care should be exercised in the selection of our assistants. No apprentice to the business of apothecary should be taken for a less term than four years, unless he has already served a portion of that time in an establishment of good character. Assistants should invariably be entered as students in a College of Pharmacy and encouraged to secure a thorough education. As the progress of our profession, in the scale of scientific attainment, must depend mainly upon those who are yet to enter it, it is recommended that those applicants who have had the advantage of a good preliminary education including the Latin language, should be preferred."

This also needs revising after twenty years of changing practice, although no improvement can be made in the underlying principles, which are fundamentally sound and worthy of perpetuation.

In 1852 our own American Pharmaceutical Association contributed its share toward the guiding principles of pharmacy and the code of ethics which was drafted during the first year of our organization was at first framed in the following language:

"CODE OF ETHICS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

"The American Pharmaceutical Association, composed of Pharmaceutists and Druggists throughout the United States, feeling a

strong interest in the success and advancement of their profession in its practical and scientific relations, and also impressed with the belief that no amount of knowledge and skill will protect themselves and the public from the ill effects of an undue competition, and the temptations to gain at the expense of quality, unless they are upheld by high moral obligations in the path of duty, have subscribed to the following Code of Ethics for the government of their professional conduct.

"Art. 1. As the practice of pharmacy can only become uniform by an open and candid intercourse being kept up between apothecaries and druggists among themselves and each other, by the adoption of the National Pharmacopœia as guide in the preparation of official medicines, by the discontinuance of secret formulæ and the practices arising from a quackish spirit, and by an encouragement of that *esprit de corps* which will prevent a resort to those disreputable practices arising out of an injurious and wicked competition; Therefore, the members of this Association agree to uphold the use of the Pharmacopœia in their practice; to cultivate brotherly feeling among the members, and to discountenance quackery and dishonorable competition in their business.

"Art 2. As labor should have its just reward, and as the skill, knowledge and responsibility required in the practice of pharmacy are great, the remuneration of the pharmaceutist's services should be proportioned to these, rather than to the market value of the preparations vended. The rate of charges will necessarily vary with geographical position, municipal location, and other circumstances of a permanent character, but a resort to intentional and unnecessary reduction in the rate of charges among apothecaries, with a view to gaining at the expense of their brethren, is strongly discountenanced by this Association as productive of evil results.

"Art. 3. The first duty of the apothecary, after duly preparing himself for his profession, being to procure good drugs and preparations (for without these his skill and knowledge are of small avail), he frequently has to rely on the good faith of the druggist for their selection. Those druggists whose knowledge, skill and integrity enable them to conduct their business faithfully, should be encouraged, rather than those who base their claims of patronage on the cheapness of their articles solely. When accidentally or otherwise, a deteriorated, or adulterated drug or medicine is sent to the

apothecary, he should invariably return it to the druggist, with a statement of its defects. What is too frequently considered as a mere error of trade on the part of the druggist, becomes a highly culpable act when countenanced by the apothecary; hence, when repetitions of such frauds occur, they should be exposed for the benefit of the profession. A careful but firm pursuit of this course would render well disposed druggists more careful and deter the fraudulently inclined from a resort to their disreputable practices.

"Art. 4. As the practice of pharmacy is quite distinct from the practice of medicine, and has been found to flourish in proportion as its practitioners have confined their attention to its requirements; and as the conduction of the business of both professions by the same individual involves pecuniary temptations which are often not compatible with a conscientious discharge of duty; we consider that the members of this Association should discountenance all such professional amalgamation; and in conducting business at the counter, should avoid prescribing for diseases when practicable, referring applicants for medical advice to the physician. We hold it as unprofessional and highly reprehensible for apothecaries to allow any percentage or commission to physicians on their prescriptions, as unjust to the public, and hurtful to the independence and self respect of both the parties concerned. We also consider that the practice of some physicians, (in places where good apothecaries are numerous), of obtaining medicines at low prices from the latter, and selling them to their patients, is not only unjust and unprofessional, but deserving the censure of all high-minded medical men.

"Art. 5. The important influence exerted on the practice of pharmacy by the large proportion of physicians who have resigned its duties and emoluments to the apothecary, are reasons why he should seek their favorable opinion and cultivate their friendship, by earnest endeavors to furnish their patients with pure and well-prepared medicines. As physicians are liable to commit errors in writing their prescriptions, involving serious consequences to health and reputation if permitted to leave the shop, the apothecary should always, when he deems an error has been made, consult the physician before proceeding; yet in the delay which must necessarily occur, it is his duty, when possible, to accomplish the interview without compromising the reputation of the physician. On the other hand, when apothecaries commit errors involving ill conse-

quences, the physician, knowing the constant liability to error, should feel bound to screen them from undue censure, unless the result of a culpable negligence.

"Art. 6. As we owe a debt of gratitude to our prodecessors for the researches and observations which have so far advanced our scientific art, we hold that every apothecary and druggist is bound to contribute his mite towards the same fund, by noting the new ideas and phenomena which may occur in the course of his business, and publishing them, when of sufficient consequence, for the benefit of the profession."

In this code, which so evidently needs revising so as to make it accord more fully with present conditions and practices, we see that the term "apothecary" is used throughout to mean a pharmacist dispensing and selling at retail, while the term "druggist" refers invariably to what we now term the wholesaler or wholesale druggist.

Slight changes in phraseology were made in this code in the first year and the amended code as published in Vol. II (153), Proc. A. Ph. A., is still in force and has not been published within recent years, except in connection with the address of Dr. Frederick Hoffmann, delivered at the semi-centennial of the American Pharmaceutical Association in Philadelphia in 1902, and published in the Proceedings for that year, and also in the JOURNAL OF THE A. PH. A., 1915, at which time a committee was appointed to revise it, which has never since reported.

Shortly after this time a very comprehensive and excellent contribution to the subject of pharmaceutical ethics was presented to the British Pharmaceutical Conference by Joseph Ince in 1866. It is well worth publishing in connection with the other data on this same subject and is particularly interesting because of the originality of some of the views and the interesting comments upon prevalent customs.

It is as follows:

"THE ETHICS OF THE SHOP.

"Pharmacy is a trade. When a man buys goods at one price to sell them at another, gaining the advantage of the difference in tariff, being further influenced by the known law of supply and demand, he is engaged in trade. When he buys in undivided bulk,

to sell again in undivided bulk, he is a merchant, but still engaged in trade. When he purchases in undivided bulk to vend in large though in divided bulk, he is a wholesale tradesman. When he buys articles in a divided bulk, to sell again in small divided bulk, he is a retail tradesman; nor does it make the slightest difference whether he sells hats or Turkey rhubarb, nor whether the seller of the rhubarb be Sir Humphry Davy.

"The artist, on the other hand, is a professional man. One painter buys so many feet of canvas, together with so much paint; he places, possibly, upon that canvas something which may not increase its value. A second buys the same amount of canvas, inch by inch, on which he puts the same amount of color, ounce for ounce, and the result may be 'The Immaculate Conception.'

"He places on the canvas that which he cannot buy—God gave it him, and without any phrase of poetry he exercises the gift divine. Neither is the true artist influenced by the necessities of competition, nor by the trade fluctuation arising from supply and demand.

"A hundred artists more or less would not alter his position; a hundred paintings on the same subject would not detract from the merit of his own, its value is intrinsic, and not relative. But the pharmaceutist buys his stock, whether of drugs, chemicals, or sundries, in order to sell again—he is a tradesman.

"But other influences are at work to modify the general fact—the awakening claims of universal education, the long unfaltering teaching of our own Society, the actual pressure from without. Then there is the influence of locality; the West End customer will have more than shop dexterity, and in my own neighborhood the mere tradesman would find himself gazetted.

"There is the influence of individual character. The master, fortunately for himself and those around him, has higher than trade instincts, from which circumstance his trade assumes more or less a strictly professional character; but it no more ceases to be a trade than the orchid which counterfeits so strangely shapes of natural beauty ceases to be a plant.

"Never forgetting the essentially trade nature which belongs to pharmacy, we at once come to the first ethical rule of the pharmaceutist, namely, the necessity for the absolutely genuine character of his drugs. No drug or remedy should be admitted

into his shop other than that which, in case of dangerous illness, he would not hesitate to supply to the inmates of his own family circle. He cannot be expected to keep the whole range of Materia Medica, nor is he to be blamed for applying for eclectic remedies elsewhere. This is an affair of means and circumstances; but in no case should any trade casuistry induce him to lower the standard of excellence of whatever he may possess.

"The pharmaceutist who bears this rigidly in mind will be in no danger of degrading himself by the adoption of low and ruinous prices. Whoever has committed this transparent trade mistake must not afterwards blame the public for exacting the continuance of a state of things to which he has himself voluntarily stooped. On this topic I have great pleasure in giving you the opinion of your excellent treasurer, Mr. Brady:—'The principle which ought to guide the pharmaceutist in the regulation of his charges is that remuneration should increase in proportion as the class of article makes greater demand on the knowledge obtained by his professional education. If he sells articles dealt in by other classes of tradesmen, he must submit to the same rate of profit. In drugs proper, which require an educated judgment, power of testing and the like, he is entitled to a much higher rate; whilst in all matters of dispensing, his charges should be professional in their character, and not calculated on the cost of employed materials at all. We cannot materially increase the quantity of medicines sold by reducing the price; hence any of us endeavoring by low charges to increase his business must recollect that he does it to the direct injury of the body, in reducing by so much the amount of money that might accrue from its legitimate practice. In large towns the responsibility of prices charged rests with one or two leading men, and if they are true to their professional instincts, the calling can scarcely fail to prosper.'

"I agree with the above, and I may add that the pharmaceutist saves himself an immensity of trouble, and will most probably prolong his days if he will once have the courage to adopt one uniform fixed price, else he is subjected to continual petty annoyance. Having determined to be the master of his own business, he will be content to abide by his own regulations, and not, on the one hand, place himself at the mercy of the competing pharmaceutist who trims his sail to every wind that blows, or, on the other,

to the caprice of the customer, who not always truthfully asserts that he has obtained articles of definite commercial value at a starvation price.

"Not only his regard to self-respect, but to his trade interest, will be his guide to a third ethical observance, *viz.*, to supply the public with the precise articles for which they ask. This point strikes me not so much as a question in ethics as in a purely business light; but I have been requested to bring it forward, and I am bound to do so.

"The rule of every well regulated establishment is to supply faithfully and implicitly whatever in the whole range of pharmacy a customer may require—to obtain it if not in stock, whether English or foreign, and to spare no pains that it shall be the identical thing desired.

"To do otherwise seems to me not to warrant so fine a phrase as a trade error, but a pure shop mistake. Does the customer want liquor bismuthi, Schacht, he is supplied from Clifton; does he send for Brown's chlorodyne, he receives that made by Mr. Davenport; if quinine be ordered, salicine must not be substituted; and so with the list of similar preparations, whether demanded as a retail order, or as forming an ingredient in a physician's recipe. This course of action is due not to any particular keen sense of honor, but to trade expediency, precisely as a wise fisherman spreads a well-made net in order that the fish should not slip through. Any house in town or country adopting such a principle must and does gain a reputation which infinitely counterbalances the small extra remuneration to be made out of fictitious articles. Confidence brings trade, and trade puts money in the till—a more practical result than might have been anticipated from the study of pharmaceutical ethics.

"This subject may have been proposed in consequence of some of its details not having been clearly grasped. On the one hand, there is a great waste of misapplied ingenuity in the constant attempt to produce colorable imitations of preparations, secret or otherwise, which have gained reputation for some particular chemist. Against this there is no human law; but the moral law, which is the law of God, says such practices are fraudulent, and beneath the dignity of every upright man, and they betray a paucity of inventive power, and it is, moreover, certain that the same skill

might find more creditable as well as more remunerative employment.

"Still, some pharmaceutists are in bondage to a groundless fear; they hesitate, under a strained sense of honor, to enter upon what they think preoccupied, and therefore forbidden ground. 'Why,' writes Mr. Giles, 'should there be any speciality in pharmaceutical production? The same laws will protect an invention in pharmacy as in mechanics, and when the law professes to deal with the matter, it is a question whether any other protection is needed. You may say ethics shall do what the law does not, and so it should in cases too refined for the law to deal with; but here the law does operate.'

"From the foregoing it is clear that while no one is justified in the fraudulent imitation of a patent right, either in or out of the sale of pharmacy, yet no pharmaceutist can claim the exclusive manufacture of any special article in perpetuity, simply because a particular mode of working originally suggested itself in his mind. There is no law in trade or ethics to prevent a man making liquor opii to the best of his ability, any more than in the case of morphia and meconic acid. The most scrupulous and conscientious chemist may get quinine and cinchonine from bark. What casuistry shall assign an arbitrary limit forbidding him to make a liquor? The whole world may make magnesia, light and heavy, calcined or carbonate, although Battley and Howard and Henry have been beforehand in the field. Let not the pharmaceutist shrink from the lawful use of the experience and labors of the past; which is no reason why he should shrink into a mere copyist, and should not, like Columbus, sail out of the beaten track in search of land not hitherto discovered.

"There is a major ethical consideration that can only be treated in a minor key—perfect civility to, and careful attention to the smallest wants of the poorest customer—a civility that should be expressed by words and manner. The ethics of civility to rich customers need scarcely be discussed; in that case, for ethics, read advantage.

"Our American brethren have taken the lead in drawing up a regular Code of Ethics. You will find the document in the *Pharmaceutical Journal*, Vol. XII, p. 369.

"They have also, I think, been most successful in giving directions about the last topic I have to mention in connection with shop ethics—the mutual relation between the master and the assistant.

"For general rules I refer you to a paper republished in our *Journal,* called the 'Pharmaceutist as a Merchant' (Vol. VI, p. 655, second series). The idea is admirable, and the literary execution quite equal to the design.

"Mr. Frederick Stearns, the author, seems to have steered most successfully between the Scylla of the high and dry, and the Charybdis of the goodly-good.

"I refer you also to some excellent rules published at the end of 'Parrish's Practical Pharmacy;' it contains one difficult proposition, p. 676.

" 'Second General Regulation of the Store. During business hours all hands must be on their feet.'

"Rule XIII is beyond our present standard. 'Every apprentice will be expected to become a graduate of the College of Pharmacy, and will be furnished with tickets of the College, and every opportunity for availing himself of the honor of the degree of that Institution.' I do not feel called upon to dilate upon this question. There is such a wide difference in individual character, that special rules seem to be impossible. After all, we shall scarcely get further than the inspired direction. 'He that ruleth with diligence.' One point I am compelled to notice, that ethics concern the assistant quite as much as they do the master. I have no intention of adding to the already hard position of the former by harsh remarks, but I say deliberately that neither our current literature, nor the general tone of sentiment expressed in private, bears sufficient trace of the recognition that a code of ethics extends beyond the master. Let the assistant feel that he has a part to play, just as difficult and just as important as his employer; that on his side he must exercise consideration, and adopt the high tone of feeling which characterizes the English gentleman, and he will do more to render pharmacy endurable, and to promote its social welfare, than whole reams of essays written on the subject. It is painful to recollect that those identical assistants who complain the most bitterly about long hours, close confinement and other ills incident to pharmacy, are sometimes, when once in business on

their own account, the very men to perpetuate and extend the evil and, practically, to rivet another link to that chain with which we are darkly bound. Solely for this reason, I have no faith in the efforts that have been made occasionally with regard to early closing. The ethics have been invariably on one side. Once the king of animals was asked his opinion on a work of art. The painting represented a man smiling and self-confident, who, with the most perfect equanimity, was slaying the noble beast. 'Wait till I paint,' said the lion.

"As matters stand, masters are to shut up, and assistants to improve their minds. I have never seen my way out of this question (nor has any one else); yet I believe that in an establishment where there are two or more assistants, if they would calmly set to work to see how far earlier hours could be adopted without injuring existing business, if, in so doing, they on their part would carefully weigh the master's interest, and be as ethical towards him as they wish him to be towards them; and if, instead of calling him hard names and making excited speeches at a London tavern, they would bear in mind that he is quite as much interested as they, I guarantee that he would be found a willing listener, and there would then be the first and only fair chance of which I know, of both being set at liberty at more rational hours than they are at present.

"Before leaving the shop altogether, may I press upon your consideration the desirability of calling it 'a pharmacy.' The word is English, not fanciful; it is used in the same sense throughout France, and Belgium, is highly expressive, and is on all grounds to be recommended."

(*To be Continued.*)

SOME APPLICATIONS OF THE MICROSCOPE IN RESEARCH.*†

By HENRY LEFFMANN, A. M., M. D.

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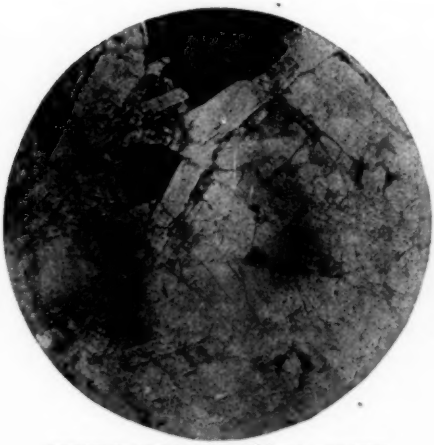
The microscope in its present form is one of the most perfect and useful instruments available in research. Its construction may be said to date from the closing years of the seventeenth century, although the general idea of magnification by curved glasses and mirrors was applied long before. While magnification is the basis of the instrument, its usefulness would be much restricted if that property alone was available. Newton's discovery of the composite nature of light gave a strong impetus to both practical study and theoretic suggestion in connection with all forms of optical instruments. Newton believed that refraction and dispersion were commensurate in all cases, and declared that it was impossible to construct a lens which would produce a colorless image. It was discovered, however, that substances of the same refractive often have different dispersive powers and Dolland was able to construct a lens capable of forming a colorless image of an object illuminated by white light. These "achromatic" lenses are now part of all microscopic outfits.

The essential function of the microscope is to make small objects visible to the human eye, but *definition,* that is, the clear indication of form and structure, is also essential, and the later work of improving the microscope is directed especially to securing this. It has been accomplished partly by improvements in lenses, but largely by modifications in the nature of the light and the method of applying it. The most simple modification is that of changing the direction of the beam that illuminates the object to be examined. The natural way, which was at first used, is to allow the beam to pass directly through the object, that is, perpendicular to it, or to fall upon the surface at a similar angle. By passing the ray obliquely, or concentrating it as a cone centering in the object, shadow effects are produced which are often very satisfactory.

*Abstract of a paper presented at a meeting of the Section of Physics and Chemistry held Thursday, October 27, 1921.

†Reprinted from *The Journ. of the Franklin Instit.*, January, 1922.

The application of photography to microscopy has been of great service, as it not only permits of permanent record of the field, but as the photographic plate has a different sensitiveness to light than has the human eye, differences of structure will be brought out by this means that the unaided eye would overlook. The ordinary photographic emulsions are not sensitive to green, yellow or red light. By special methods this sensitiveness may be extended so that a strong light of any color will affect the plate. Using plates of wide range of sensitiveness, color screens can be inserted by which excellent results are often secured. Another modification of light which has been of immense advantage in all fields of optics is polarization. The term is applied to modifications of light by which



SECTION OF DOLERITE × 30. WHITE LIGHT.

SECTION OF DOLERITE × 30. RED SCREEN.

it becomes much more sensitive to structure so that differences wholly inappreciable to the unassisted eye are brought out clearly. These differences are often indicated by brilliant colors, so that the several parts of the object are not only clearly indicated but the color contrasts are striking and often beautiful.

Another direction in which the service of the microscope has been advanced is in the preparation of the object. Many methods for this purpose are employed. One of the most used is sectioning, that is, cutting the specimen into thin layers. In the case of animal and vegetable structures this is comparatively easy, and has been employed from an early period, but mineral structures are more dif-

ficult to handle. Sorby, a British scientist, developed about the middle of the last century the method of grinding minerals so thin as to be transparent, and laid the foundation of the science of petrology which has become of great importance in mineralogy and geology. In the case of metals no amount of cutting will render them transparent to ordinary light, but many important data have been obtained by examining flat surfaces before and after etching. A special department of industrial microscopy—metallography—has grown up by aid of the methods of which the minute structure of commercial metals and alloys is capable of elucidation.

The microscope has found extensive and useful application in medico-legal work. Its revelations are often surprising and sometimes border on the humorous, because of the results being so different from what was assumed. During the late war cases of admixture of powdered glass with food were occasionally alleged. No case in which such a charge was substantiated seems to have been established, but several investigators have reported the actual facts. In one case crystals of ammonium magnesium phosphate were found; in another, in which it was suspected that grape-jelly had been so adulterated, the analyst (Doctor LaWall) found that the substance was merely cream of tartar (acid potassium tartrate) in comparatively large crystals. The client, however, was firm in his opinion, and it was not until the analyst dissolved some of the material in hot water that he was convinced it was not glass.

Messrs. Zoller and Williams, of the United States Bureau of Agriculture, recently reported a case of "sandy" ice cream, which on microscopic examination was found to owe its grittiness to numerous crystals of milk sugar. Commercial white arsenic (arsenous acid), the common poison, is found in two forms, a glassy or porcelain-like mass and a gritty powder. The latter generally shows distinct crystals, visible under moderately high powers, the particular form being the regular octahedron, but much broken up. This form of arsenic will remain for many hours in the stomach without material modification so that the substance may be identified directly. In one case of criminal poisoning, the defence set up the theory that the dead person had been taking homœopathic triturations of arsenic, but the expert for the state pointed out that the arsenic found in the stomach was distinctly crystalline, which proved that it had not been triturated. The prisoner was convicted and executed, and subsequently

his attorney admitted the correctness of the inference, and the remainder of the arsenic, which had been bought for the poisoning, was given to the expert.

By making thin sections of fossils and coal much information may be obtained as to the origin of these materials. Coal shows vivid evidence of its vegetable origin, not only by the impressions of leaves and stems, that are visible to the naked eye, but on magnification, the minute details of the cell structure and spores. Considerable advance has been made lately in the study of coal, by treatment with hydrofluoric acid, by which the mineral matter is in great part removed, and thus the remains of the vegetable structures made more evident.

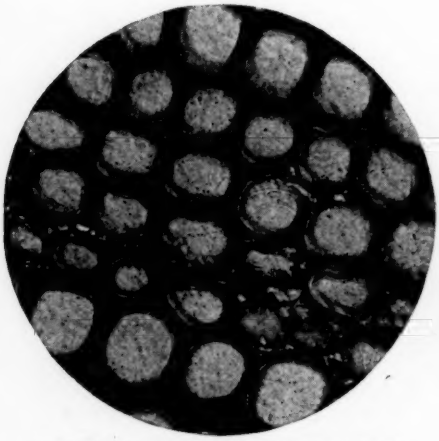
SECTION OF COAL × 120. SHOWING VEGETABLE CELLS.

CRYSTAL OF MILK SUGAR × 100.

The fossil tree-trunks in the petrified forests of Arizona have retained the vegetable structure through the solidification, even to very minute detail, and by the microscope it can be shown that they are cone-bearers, related to our pines and spruces. They show clearly the peculiar dotted cells, technically known as the "bordered pits" which are characteristic of that group of plants.

In the field of pathology and bacteriology the microscope has been of immense use. Its applicability has been materially increased by the use of cultures and staining systems. The invention of the solid culture medium, by Doctor Koch, has been one of the most important accessories in this work. Micro-organisms can be cultivated

in many liquids and on many surfaces, but the different species remain in intimate mixture and study of individual forms is impossible. By incorporating into the culture fluid a substance which is liquid when moderately warm, but solid at ordinary temperatures, the organisms can be cultivated separately. Gelatin and agar are usually employed, the latter being especially applicable for cultures made at blood heat, as its jelly does not melt at that temperature. The procedure, in outline, is to prepare a sterile culture medium containing the jelly-forming substance, inoculate under proper precautions, spread it in a shallow dish, and cover it with a protecting



TRANSVERSE SECTION OF PETRIFIED WOOD. PETRIFIED FOREST OF ARIZONA × 120.

SECTION OF PETRIFIED WOOD × 120. SHOWING "BORDERED PITS" WHICH INDICATE CONE-BEARING TREE.

lid. When cold the jelly sets, and the individual organisms multiply in their places, soon forming colonies so numerous that they are large enough to be seen by the naked eye. In growing, some organisms produce marked changes in the condition of the gelatin or agar. Some digest it partly, causing spots of liquid, others produce colors. One well-known and common organism produces a blood-red stain. From the colonies thus indicated, portions can be taken and separately cultivated, just as one can gather seeds from the mature plants of a garden.

One of the latest applications of the microscope is its use in determining the index of refraction. This datum is the expression of the amount to which the ray of light is bent on passing from air

into the mass of the substance under examination. The figure for the index is obtained by dividing the sine of the angle of incidence by that of the angle of refraction. In dealing with solids and liquids as compared with air the quotient is, of course, always greater than unity. Differentiation of both solid and liquid substances can be made rapidly and accurately by determinations of this index. In microscopic work, the method is largely applied in examining crystals.

In examining substances more or less transparent immersed in a liquid, the individual particles are seen to be surrounded by a series of bands either in monotone or in colors. The relative extent of these bands depends on the difference between the refractive index of the substance and that of the liquid bathing it. If the objects examined are entirely homogeneous, without color, have the same refractive and dispersive powers, and also the same absorptive powers for light as the liquid, they will become invisible. All these conditions as coincident are not found in practice, so there is always some visibility. In practice the vanishing of the dark bands is the phenomenon that is used to aid in the examination. If, for instance, a crystal is examined successively in liquids of which the index of refraction is known, it is possible to determine that of the solid, by noting the liquid in which the dark bands are just eliminated.

By these means crystals of very small size can be identified and many interesting and valuable results have already been obtained. Dr. Edgar T. Wherry, of the United States Bureau of Chemistry, has for several years been devoting a great deal of attention to this phase of research and has made many determinations. One of the most interesting and valuable was in the detecting of the cause of mortality among bees in some parts of Pennsylvania. The honey on being examined was found to contain crystals of unusual form, and as the amount was very small resort was had to the determination of the index of refraction, by which the substance was identified as melezitose, a sugar that is of no nutritive value to the bee. This had been obtained probably by the bees collecting exudations on pine trees, during a period in which flowers were scarce. Doctor Wherry made also examinations of some high explosives which were of different colors as produced in different factories and found that the difference was due to enclosures in the crystals.

Efforts have been made of late to apply the refractive index to the differentiation of the common alkaloids. Some of these are powerful poisons, and as they are used in small amount the processes of analysis have to be very delicate. Many of the tests depend upon color produced by reagents, but in these the alkaloid is destroyed. The crystalline forms of the alkaloid itself or of its salts are sometimes fairly characteristic, but as a rule such method is only applicable to the pure substance. In toxicologic analysis the material is often difficult to obtain perfectly pure, and this complicates the work. Naturally the determination of the refractive index seems to be a possible method, but one difficulty has arisen, namely, to secure liquids which do not have a solvent action on the crystal. It is obvious that if the substance dissolves in the liquid bathing it, no accurate test can be made. Human ingenuity is, however, almost limitless, and it is reasonable to expect that some method will be found by which this useful datum will be made available for the toxicologist and pharmacologist in identifying these important substances.

ACETYL-SALICYLIC ACID IN SODIUM CITRATE SOLUTION.*†

By Paul Nicholas Leech, Ph. D., Chicago.

Acetylsalicylic acid ("aspirin") is dispensed in dry condition because it is easily decomposed in the presence of moisture; also it is insoluble in water. However, articles have appeared recently in both medical and pharmaceutic literature claiming that acetylsalicylic acid may be dispensed *in solution* by aid of sodium citrate; also that the acetylsalicylic acid would not be decomposed. For instance, the following, which was probably abstracted from some American pharmaceutic publication, appeared in the *Prescriber*:[1]

"Acetylsalicylic acid (aspirin) is practically insoluble in water, and though soluble in alcohol such a solution is not generally suitable for administration. It is therefore usually given in tablets or

*From the Chemical Laboratory of the American Medical Association.
†Reprinted from *Journ. Amer. Med. Assoc.*, January, 1922.
[1] Solvent for Acetyl-Salicylic Acid, *The Prescriber*, June, 1921, p. 247.

cachets. Solution may be effected by addition of sodium bicarbonate, but as the resulting solution is merely a mixture of sodium acetate and sodium salicylate, this method is not admissible. It is said that sodium citrate will dissolve acetylsalicylc acid without dissociation; for each grain of aspirin four grains of sodium citrate should be added. Such a solution, flavored with syrup of lemon, is suitable for administration to children.

The usual test for decomposition of acetlysalicylic acid is the detection of the freed salicylic acid by means of ferric chlorid solution. It occurred to me, therefore, that possibly such a test was used as a basis of the contention of the non-decomposition of acetylsalicylic acid in sodium citrate solution. If so, the seemingly negative reaction obtained may be misinterpreted, because citric acid, and citrates, interfere with the sensitiveness of the test, and hence it would not be reliable in the case at hand. To test this hypothesis, a solution was made up and the rate of hydrolysis determined by titrating with normal alkali during stated intervals. The solution was prepared by dissolving about 18 gm. of pure acetylsalicylic acid and 72 gm. of sodium citrate in 240 cc. of water; after standing three hours it was filtered, and 20 cc. used for the individual determinations. One teaspoonful of such a solution would represent about 5 grains of acetylsalicylic acid. The results of the titration will be found in the accompanying table. The solution was maintained at room temperature.

RESULTS OF TITRATION.

Interval of Time.	Cc. of N/1 NaOH Consumed by 20 cc. of Solution.
3 hours	8.0
1 day	9.4
2 days	10.7
3 days	11.35
3⅝ days	11.80
6 days	12.70
9 days	13.80
14 days	14.85
17 days	15.20
Complete hydrolysis	15.70

Acetylsalicylic acid is hydrolyzed fairly rapidly in sodium citrate solution, over 50 per cent. decomposed in four days, and 75 per cent. in nine days. Thus, a patient taking such a mixture which

was nine or more days old would be getting essentially the same ingredients as if sodium acetate and sodium salicylate had been used in place of the acetylsalicylic acid.

Obviously, the assertion that acetylsalicylic acid is not broken down to form salicylic acid and acetic acid (or their salts) is not based on scientific work.

The hydrogen ion concentration of the citrate solution alone was $p_H = 9.0$; after addition of acetylsalicylic acid, it was $p_H = 5.4$; after seventeen days it was $p_H = 4.6$ Thus it may be seen that the solution is appreciably acid, sufficient to decompose hexamethylenamin, with which it has been recommended to be dispensed.

Very recently one part of potassium citrate has been suggested in place of four parts of sodium citrate. Such a solution would hydrolyze, if anything, faster than one made with a higher concentration of the sodium salt.

CONCLUSION.

It has been claimed that acetylsalicylic acid may be dispensed in a solution of sodium citrate without decomposition of the acetylsalicylic acid. The experiments here reported show that this is incorrect, that after four days the acetylsalicylic acid is broken down to the extent of 50 per cent.; after nine days, to 75 per cent., and that in seventeen days it is almost completely hydrolyzed.

THE SIGNIFICANCE OF CALCIUM FOR HIGHER GREEN PLANTS.

By RODNEY H. TRUE. *Science*, 55, 1410, 1-6, 1922.*

Interest in the subject of Calcium as a necessary plant food began to develop as far back as 1856 when Salm-Horstmar proved that this element is necessary for seed plants. Additional light was thrown on the calcium problem by Sydney Ringer in 1883, who, while working on the characteristic effects produced by various salts in prolonging the life of organisms in water culture, observed that when fish were placed in distilled water calcium and other salts were extracted from them and epithelial and mucous cells seemed to become detached from the gills. Ringer later experimented with Tubi-

*Abstracted by Heber W. Youngken.

fex, a fresh water worm, and found that after this animal was kept in water from which calcium was excluded, the worms disintegrated and when calcium was added to distilled water the worms lived and behaved as in river water. Herbst in 1900 confirmed the fundamental features of Ringer's work, when he showed that in certain sea-urchin larvæ grown in sea water from which Calcium was lacking the epithelial tissues dissolved into their component cells and that when these dissociated but still living elements were returned to calcium containing sea water, they adhered again to each other at their points of contact.

The author reviews the work of himself and colleagues on the physiological properties of distilled water in which the method of electrical conductivity was applied to the investigation of ion changes in solutions in which seedlings were growing. These experiments demonstrated first, that the conducting capacity of distilled water in which seedlings were grown increased, due chiefly to the leaching of ions from the cells of the seedlings, second that this leaching was checked when a small quantity of Ca salt was added to the distilled water, third, that Ca ions differed from Mg ions in being harmless in concentrations that proved fatal in the case of Mg.

Dr. True also relates how the conducting method was next applied to the problem of absorption by phanerogamic seedlings from solutions of the ordinary nutrient salts. As a result of the study of various kinds of seedlings grown in solutions of single salts it was found that in solutions of K and Na salts no concentration was observed in which the seedlings were able to carry on sustained absorption. In the end the seedlings yielded more ions to the medium than they took from it. Again, it was found that in mixtures absorption or leach depended on the presence of Ca or Mg ions. Calcium in high proportion never brought injury and Mg injury appeared less often than in single solutions. It was further noted that in mixtures containing Ca and other nutrient ions, the total quantity of ions absorbed far exceeded the quantity of Ca ions present. This showed that in such mixtures Ca ions in some way secured conditions that bring about the absorption of ions which, when offered in unmixed solutions, would be unabsorbable or would cause an active leach of other ions from the plant cells.

The author thus logically concludes that the Ca ions make other ions physiologically available to the plant.

The author next takes up the question of the chemical relation between the calcium content of higher plants and the cell wall. He cites the investigations of Fremy, Mangin, Bertrand and others who showed that cell walls were not homogeneous structures but consist of an outermost boundary layer between adjacent cells of a calcium salt of a weak organic acid known as pectic acid as well as other layers lying between it and the plasma membranes. Ca pectate is a stiff adhesive colloid that is formed when Ca ions meet pectic acid. Pectic acid appears when the neutral substance pectin is acted on by the enzyme pectase. He further cites Sampson's observations of how cellulose cell walls in the abscission tissue of Coleus leaves are changed to pectic acid with the disappearance of calcium ions from the cells and walls following injury. He calls attention to the change in firmness of fruits and vegetables following the action of saprophytic or parasitic fungi as being likely due to the removal of Ca by acids, the pectate layers becoming pectic acid or something akin.

He next reviews the work of Dr. Sophia H. Eckerson, who in 1919-20 grew seedlings of wheat, maize and white lupine in a series of balanced solutions and who applied microchemic methods to the study of seedlings grown in potassium solutions in which the author had found a leaching of ions from the seedlings into the solution. This work demonstrated (1) that ions readily enter the cells of the roots, (2) that within 24 hours Ca ions began to diffuse out of the calcium pectate middle lamella, (3) K pectate was formed instead of the Ca salt and this substance being relatively soluble in water soon dissolved, (4) at this stage, sugars, amino-acids, and salts, chiefly Mg, diffused rapidly out of the roots. The leach into K solutions is largely organic and non-electrolytic showing the solutions to have come in considerable part from the cell contents. The permeability of the cell walls had so been greatly modified as well as the osmotic properties of the plasma membranes.

Experiments on corn seedlings by the same worker showed that permeability for ingoing ions is likewise increased by the changes described. Experimental work on Mg solutions showed that Mg pectate replaced Ca pectate in solutions of Mg salts. After examining the results of a long series of experiments in various culture solutions, the author declares that no kation other than Ca has been found that can replace it in the colloidal compound forming the mid-

dle lamella without an injurious or fatal change seen in permeability relations or without the appearance sooner or later of other toxic response.

In view of the results cited, the author next philosophizes on the phenomena lying deeper than the cell walls. He regards the cell walls and plasma membranes that secrete it as standing in the closest relation. He states: "Cell walls, except in specialized locations, are seldom decisive in determining what ions pass through them. They influence up to a certain quantity the ions that pass into them, through the chemical changes which take place in the walls themselves. Beyond that, after chemical demands in the walls have been satisfied, more deeply lying equilibria are concerned. As an ion-containing structure, the cell wall maintains ion-equilibria subject to the laws of equilibria in colloids, with the living membranes with which it stands in most intimate chemical and biological contact. When ion equilibria in the wall are disturbed, this disturbance is transmitted to the equilibria of the protoplast that lays it down, modifies it and remains in closest relation to it."

As an example of emphatic control of cell walls by life inhabiting them, he cites the condition in the developing fruits of wheat and maize.

The embryos of these normally have a dozen or more cells surrounding them. In response to intrinsic or formative laws governing the organisms, these cells are completely absorbed and in the end the innermost remaining walls of the ovary are cemented to the outer unabsorbed layer of the inner integument. He claims this control to be exerted chiefly through the agency of the Ca-ion equilibria of the tissues concerned.

The substances necessary for the formation of the cementing layer appear, according to Dr. True, to be extruded from the protoplasm through the wall to the outside surfaces where they unite to form the coagulum. It is conjectured that Ca ions and pectase thrust through from the interior of the cell meet at its frontier the pectin which under enzyme action yields pectic acid that then unites with Ca ions to form the cementing calcium pectate layer between adjacent cells.

In conclusion the author points out the fact that calcium ions make physiologically available other equally indispensable nutrient ions and alludes to this as clearing up some previously unsolved questions.

ATOMIZING THE ATOM.

(Reprinted from *Science Service.*)

How one element can be changed over into another was explained recently to the Chemical Society of London by Professor Sir Ernest Rutherford, of Cavendish Laboratory, Cambridge, who has gone farther than any other man toward realizing the old dream of the alchemists.

We are as far off as ever from the making of gold out of lead, but experiments by Professor Rutherford have previously shown that it is possible to get hydrogen out of nitrogen.

Professor Rutherford declared that it is also possible to obtain hydrogen from at least five other elements, boron, fluorine, sodium, aluminum and phosphorus.

These experiments have given us an entirely new idea of the structure of the atom. As Professor Rutherford says: "Since the development of the atomic theory on an experimental basis by Dalton, the progress of chemistry has been based on the central idea of the permanency and indivisibility of the atoms of the elements. The whole experience of chemistry for nearly a century had shown clearly that it was impossible to break up the atoms of the elements by the application of ordinary chemical and physical processes. This idea has had to be modified to some extent by the rapid growth of our knowledge during the last twenty years of the inner constitution of the atoms. It is now generally accepted that the atoms of the different elements have all the same general type of structure. At the centre of the atom is a positively charged nucleus of minute dimensions which is responsible for most of the mass of the atom. This is surrounded by a distribution of electron held in equilibrium by the forces from the nucleus.

"By the action of light and electrical discharges, we can readily remove one or more of the external planetary electrons from the atom, while by the action of X-rays we may even eject one of the more strongly bound electrons of the system. In this way, we can effect in a sense a transformation of the atom but it is merely a temporary one and a new electron is soon captured from the outside and the atom is as before. The general evidence indicates that even if a number of the planetary electrons were removed by suitable

agencies the stability of the nucleus would not be disturbed and the atom would in a short time regain its original structure. In order to effect a permanent charge in the atom it appears to be necessary to disrupt the nucleus itself. When once a charged unit of the nuclear structure is removed, the nuclear charge is altered permanently and there is no evidence that this process is reversible under ordinary experimental conditions.

"The discovery of the instability of the radioactive elements was the first severe shock to the idea of the permanency of all atoms. This radiating property is, however, confined mainly to the two heaviest elements, uranium and thorium, and their long series of descendents, and is only shown by two other elements, potassium and rubidium, and then only to a minor extent. Apart from these exceptions, the great majority of the atoms appear to be highly stable structures and to remain unaltered under ordinary conditions in this earth for periods of probably thousands of millions of years.

"The property of radioactivity belongs to the nucleus and is shown generally by the emission of a swift particle or helium nucleus and occasionally a swift electron from the nucleus. The number and velocity of emission of these particles appear to be quite uninfluenced by the most powerful physical or chemical agencies and to be an inherent property resulting from the instability of these very complex nuclei.

"These results show clearly that the nuclei of heavy atoms contain both positively charged helium nuclei and negative electrons, and lead to the general view that the complex nuclei of all atoms are built up of hydrogen and helium nuclei and electrons. It is also generally supposed that a helium nucleus itself is a secondary unit composed of four hydrogen nuclei and two electrons. If this be the case, we may suppose the nuclei of all atoms to be composed ultimately of hydrogen nuclei, or protons as they have been termed, with the addition of negative electron.

"It is probable that the forces which bind together the components of the nucleus are exceedingly powerful and that consequently a large amount of energy will be required to disrupt its structure. The swift alpha particle from radium and thorium, which is by far the most concentrated source of energy known to us, seems the most likely agent to succeed in an attack on the strongly bound nucleus. The alpha particle is expelled from radium with a

velocity of about 10,000 miles per second and thus has a speed 20,000 times greater than that of a swift rifle bullet. Mass for mass, its energy of motion is 400 million times greater than that of the bullet."

In investigating the disintegration of atoms, Professor Rutherford makes use of the same phenomena that are displayed in the luminous watch dials made of a radioactive element bombarding zinc sulphide. He allows the particles projected from radium to bombard the element and then counts the number of electrons or hydrogen atoms that are knocked out by the flashes they produce when they hit a screen of zinc sulphide.

"If we had charged atoms available of ten times the energy of the alpha particles of radium, we could probably penetrate the nuclear structure of all atoms and occasionally effect their disintegration," states Professor Rutherford. "The general evidence indicates that the atoms as a whole are such stable structures and the nuclei are held together by such powerful forces that only the most concentrated source of energy like the alpha particle is likely to be effective in an attack on such well protected structures."

SCIENTIFIC AND TECHNICAL ABSTRACTS

THE RESIN OF KAVA KAVA (PIPER METHYSTICUM).—The resin was dissolved in ether to free it from methysticin, the ether solution was washed with dilute alkali and then with dilute sulphuric acid and was dried with potassium carbonate. Removal of the solvent left a thick, dark brown, oily residue. When this was heated with 10 per cent. sodium hydroxide solution Kavaic acid was obtained. This product is, apparently, y-cinnamal-acetoacetic acid, $C_6H_5.CH:CH.CH:CH.CO.CH_2.COOH$. Yellow needles from methyl alcohol, M.P. 164-5° (decomp.). It readily parts with CO_2 and yields a dark yellow resin which, on distillation, produces cinnamal-acetone, $C_6H_5CH:CH.CH:CH.CO.CH_3$. (W. Borsche and A. Roth, *Ber. d. d. chem. Ges.* 54, 2229, 1921.)—J. F. C.

A NEW MOTOR FUEL.—An enforced situation in Germany a few years ago, brought about by the interruption of importation of petroleum and petroleum products, reflected a condition which the world will eventually face universally, and resulted in the search and discovery of substitutes which were able to take the place of gasoline and lubricating oil in particular. This work has been described in *Auto-Technik* and *Revue des Produits Chimiques*. The Germans fell back on coal tar from which they obtained benzol and naphthalene. The former has been used as a motor fuel for some time in admixture with alcohol and gasoline. The latter, when treated with hydrogen in the presence of the catalyst nickel, gives a series of products, one of which, known as tetralin, has been used recently with great success in the operation of automobile engines. The results obtained were even better than those ordinarily secured with gasoline as the fuel, for tetralin has a high specific gravity and a much greater calorific power than gasoline. Per kilogram, this is 11,600 calories for tetralin against 11,000 for the best grade of gasoline. The tetralin is not used alone but in admixture with alcohol and benzol, in the proportion of two of the latter and one each of the former. The ordinary form of carburetor may be used, but it must be adjusted to give increased admission of air, and it is advisable to preheat the fuel with the waste heat from the engine before allowing it to enter the cylinder. It is possible to start an absolutely cold engine with this composition fuel. The mixture will not foul the spark plugs. A test was made with the fuel on a standard make of car in Germany, which was run a fixed distance with an absolutely cold engine with this composition fuel. The regular type of carburetor was used, the same one in each test. The tetralin fuel ran the car twenty miles to the gallon, while the gasoline fuel ran it twelve miles per gallon under identical conditions. This indicates an increased efficiency in favor of the new fuel to the extent of 66 2/3 per cent. The speed of the car reached 55 to 65 miles per hour.—Through *Industrial Digest*.

INSECT ENEMIES OF TYPHA LATIFOLIA.—An intensive study of the Insect Enemies of Typha latifolia L. P. W. Claassen, of Cornell University Exp. Station, has made an elaborate study of the Typha latifolia, in its habitats, and finds that it is the prey of twenty-five different insects representing five of the great orders of that division

of the animal kingdom. The species are distributed as follows: Six lepidoptera (butterflies and moths), two coleoptera (beetles), eight hemiptera (bugs), five hymenoptera (bees and wasps), four diptera (flies). The methods of attack and the life history of each insect have been carefully traced out. The several insects specialize somewhat as to the part of the plant that is attacked. Three moths and a bug are parasitic on the flowering head; the leaves are attacked on the surface and by leaf miners; the stalk is invaded by two of these leaf miners, but other species are not originally in the leaf. A few invade the rhizome, living largely upon the starch therein.

Notwithstanding its numerous enemies the plant is abundant in many parts of the world, and several parts of it have been suggested as possibly useful. Engler and Prantl speak of rhizome starch as a food supply, of the leaves as a source of textile material and of the pollen as a substitute for lycopodium. Claassen has investigated the question of using typha as a food product, and published his results a couple of years ago.—H. L.

Standardizing Biologic Stains.—Since the interruption of the supply of German staining materials, which were very accurately prepared and largely used, some difficulty has been found in getting uniform results with domestic products. Manufacturers have been willing to meet the demand, but the users of the stains have not always been precise as to their needs. The Society of American Bacteriologists recently made efforts to bring about satisfactory conditions, and still more recently, other societies have offered assistance. A conference was held in New York City last November under the auspices of the National Research Council, at which representatives from a number of interested organizations were present. After an extended discussion it was agreed to appoint a committee, which has since been named to act under the division of Biology and Agriculture with co-operation of the Division of Medicine. The Chemical Foundation of New York City has subscribed $500 towards financing the work.—H. L.

Domestic Manufacture of Synthetic Compounds.—The development of the manufacture of the many complex synthetics which are used in chemical and biologic research has reached a

gratifying point in the United States. A number of firms have devoted time and money to this work and the list of substances that can now be obtained without sending abroad is quite large. This work has naturally interested the German chemists, and even the work that is being done in creating an American literature has awakened anxiety in the land beyond the Rhine. A German review of Whitmore's monograph on "Organic Mercury Compounds" gives evidence of this in the sentence, "The war, which was ended three years ago, is to be carried further in scientific and industrial fields. In view of this one cannot welcome the publication of the monographs."

"Let the stricken deer go weep,
The hart ungalled play."

H. L.

SEPARATION OF DEXTROSE AND SUCROSE BY DIALYSIS.—Congdon and Ingersoll (*Jour. Amer. Chem. Soc.*, 1921, 43, 2588) give the results of experiments which indicate the possibility of a close analytical separation of these sugars by a simple dialytic method. They found that in mixtures the influence of the dextrose on the dialysis of the sucrose is such that within certain concentrations the ratio of the dextrose dialyzed to that of the sucrose dialyzed is such as to keep this ratio constant, irrespective of the proportion of sucrose in the original solution. In very dilute solutions of the two sugars, dextrose can be quantitatively separated from sucrose by dialysis in about fifty hours.—H. L.

MEDICAL AND PHARMACEUTICAL NOTES

CHAULMOOGRA OIL NOW USED IN TREATING LARYNGITIS.—Chaulmoogra oil, which has been bringing health to many sufferers from leprosy, is now used in the treatment of tuberculous laryngitis. Dr. R. M. Lukens, of Jefferson Hospital and Henry Phipps Institute, of this city, has treated patients for the past year by spraying the oil into their diseased larynges. While the treatment is not all that is to be desired, it is not unpleasant or distressing, and gives

better result than some other drugs previously used. Laboratory studies show that chaulmoogra oil does not kill the tubercle bacilli, but the tests on patients show a marked aid in healing diseased lesions on the organ that produces the sound when a person talks.—*Science Service.*

DIAGNOSE ILLS OF 4000 YEARS AGO.—Present-day post-mortems of human beings who lived 4000 years ago and examinations of cave bears and a crocodile who basked in the sun some 900,000 years ago have revealed the medical aches and pains of those times.

Bones of ancient life have previously given medical clues to scientists of today, but the late Sir Armand Ruffer devised methods of studying the soft tissues of the Egyptian mummies that the hot sands and dry climate of Egypt have preserved for thousands of years.

The bacteria, the diseases, and man's reaction to them have not changed during the thousands of years that have passed, he found.

The inhabitants of the Nile Valley, the cradle of history, suffered from stiffening and swellings of the joints to a far greater degree and at a much earlier age than we now see this disease. A hump-backed priest of Ammon, 1000 years B. C. owed his hump to Pott's disease, which shows how little 3000 years have altered the behavoir of tuberculosis. Bacteria in these old bodies can still be stained, and traces of pneumonia can be seen. Lesions closely resembling small pox can still be recognized and studied by modern micoroscopic methods in these old mummies. Hardening of the arteries was common and severe in those days, when tobacco, excessive meat eating, modern strenuosity, and such things that nowdays are blamed for this condition certainly did not exist.

"Men were commonly stiff and old by the time they had reached fifty years, and the good old days were not so good from the sanitation standpoint," says the *Journal of the American Medical Association* in commenting on Dr. Ruffer's late work, "and we find that royalty was of very common clay, with extremely bad teeth and gums, queens bald of head, and even, we blush to say it, princesses with nits in their hair. Syphilis has not yet been demonstrated in early Egyptian bodies, a fact which may have influenced the sociology of the day. Food habits varied from time to

time and in different classes, as shown by the degree of wearing down of the teeth, but at no time did there exist those prehistoric dentists of whom all popular histories of Egypt relate, although they certainly were sorely needed."

The best mummy material obtained is that which is naturally preserved by the Egyptian climate. The Egyptian embalmers had no such supernatural skill as tradition ascribes to them, but they did remove the vital organs of the body before burial, much to the sorrow of present medical archeologists.

Even the illnesses of the dinosaur who lived many thousands of years before the Egyptians have been investigated. Prof. Roy L. Moodie, of the University of Chicago, has found pathologic lesions on the tail of this pre-historic reptile.—(*Science Service*, February, 1922.)

CARBON-TETRA-CHLORIDE PARALYZES HOOKWORM AS WELL AS FIRE.—Carbon tetrachlorid, a common chemical, may in the future replace chenopodium, the substance now used in the removal of hookworms and ascarids in man. In the last few years, millions of people in the tropics and warmer regions have been cured by modern medical methods of the hookworm disease and the work is still in progress.

Dr. H. M. Hall, of the Bureau of Animal Industry of the Department of Agriculture, has made conclusive experiments that show that carbon tetrachloride in addition to being more effective is safer and cheaper than the drugs used now.—(*Science Service.*)

ALASTRIM, A NEW NAME FOR AN OLD AILMENT.—Alastrim, a disease that resembles smallpox, is now being studied by medical men.

It was reported in epidemic form in 1920 in the Caribean littoral, Canada and England. In the present state of knowledge of its exact classification, it is being combated and reported as smallpox.

"The disease is very infectious to man; both sexes and all ages are attacked," says Dr. W. C. Rucker, of the United States Public Health Service. "No racial immunity has been observed. The disease is found in the West Indies, South and Central America,

South Africa, the Mediterranean area, and, more recently, in Great Britain. It is probable that the so-called 'Cuban itch' and 'Philippine itch' observed after the war with Spain, the mild form of smallpox prevalent in America, and alastrim are identical. The disease is highly contagious, its causal organism being spread by both direct and indirect vection. Certain observers believe that the disease is largely spread by the air; but when the enormous number of daily contacts with fellow man is considered, the assumption of this theory to account for the rapid spread and persistence of the disease seems scarcely warranted. Overcrowding helps to spread the disease. The exact classification of alastrim is still the subject of considerable discussion. It may be, and probably is, merely a mitigated form of smallpox, which, in an environment of low racial immunity, incomplete vaccination, or lowered vitality, might regain its lost virulence. It may be that the parasite is a separate species of the parent type."

The mortality from alastrim is surprisingly low. The disease is more severe in the unvaccinated and debilitated. Economically, it is important by reason of the rapidity of its spread and the temporary disablement of large numbers of persons.—(*Science Service.*)

WITCHES' OINTMENTS.—In a work entitled "The Witch-Cult in Western Europe" by Margaret Alice Murray, published recently by the Clarendon (Oxford) Press, some formulas are given for ointments with which the witches were said to anoint themselves in order to be able to make broomstick flights. The work indicates the existence of a widespread cult of Devil-worship, and it is possible that the ointments were really used as a means of getting rid of objectionable persons. The author gives three formulas.

1. Parsley, water of aconire, poplar leaves, soot.

2. Water parsnip, sweet flag, cinquefoil, bat's blood, deadly nightshade.

3. Baby's fat, juice of water parsnip, aconite, cinquefoil, deadly nightshade and soot.

The original data are in old French, and it is possible that the words translated "parsley" and "water parsnip" may refer to more poisonous forms of Umbelliferæ.—H. L.

"SOLID EXTRACTS"

A single bill of paper money may carry as many as one hundred thousand bacteria. These are mostly of the type found in the intestines, but disease-producing bacteria may also be present.

The Vermont Experiment Station has recently shown that the number of thorns which a blackberry vine produces is determined by the amount of light which is receives. Plants grown under shade produced only a few weak prickles, while those grown in full sunlight produced their full complement of very stiff, stout spines.

CALORIFIC VALUES OF CEREALS.

(Calories per pound.)

Oat flour	1795
Rye flour	1660
Rice flour	1645
Barley flour	1640
Corn flour	1630
Wheat flour	1620

It has been demonstrated at the University of Minnesota that there are at least twenty-five distinct varieties of the stem rust of cereals and grasses.

It has been found that salts of lead, in very small amounts, will stimulate plant growth.

Spider silk is used in telescopes and various other optical instruments to indicate by cross lines points in the field of vision. Many attempts have been made to substitute spiders for silkworms in the production of silk for general use, and a small industry of this description exists in Madagascar.

A recent note in *Science* records what is believed to be the temperate zone record for a single season's growth of a shoot of the tree type of woody plant. This phenomenal shoot grew from the

stump of a beheaded Paulownia and reached a height of 21 feet 6 inches, a circumference of 10 inches at the base, and had 24 leaves, one of which, measured in late July, was found to be 38 inches long in the largest dimension.

A radish will turn its leaves toward a source of light no stronger than that of a candle twenty-five feet away, while one of the cresses is similarly sensitive to light of a strength equal to that from a candle about one hundred eighty feet away.

It will come as a surprise to many people to learn that, at the present time, the United States produces much more radium than all the rest of the world together. From the beginning of the industry in 1913 to January, 1921, approximately 115 gm. of radium element were produced in this country. Probably not more than 40 gm. have been recovered from foreign ores since the discovery of radium by Madam Curie.

For many years radium was exclusively produced from the Austrian ores at Joachimsthal; later, it was obtained from pitchblende deposits in Cornwall, and from autunite deposits in Portugal. About nine years ago, officials of the Bureau of Mines found that the carnotite deposits in southwestern Colorado and eastern Utah represented the largest bodies of radium-bearing ore in the world.

Some very sensitive tendrils will respond with a curvature to the friction produced if a bit of thread weighing about one hundred-millionth of an ounce is being blown across it by the wind.

The Abbe Theodore Moreaux, Director of Observatory at Bourges, has recently given some estimates of the age of the earth and when the phenomenon of life appeared on it. He considers 500,000,000 years about right for the age of the earth and he thinks that the temperature dropped to a point where life could exist about 250,000,000 years ago. Man was a comparative newcomer and the Abbe gives only some tens of thousands of years, thus refuting an estimate of a German scientist, who recently gave 40,000,000 years as the probable period for the advent of man.—*Scientific American.*

NEWS ITEMS AND PERSONAL NOTES

DECEASE OF WILLIAM P. CLOTHIER.—A veteran graduate of the Philadelphia College of Pharmacy passed away recently in Buffalo. Dr. William P. Clothier was one of the oldest practicing pharmacists in western New York. He was born in Philadelphia in 1839 and studied pharmacy and graduated there in 1861, when he went to Buffalo and graduated in medicine at the university of that city.

POPULAR LECTURES AT THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.—That this innovation met with the instant success which the project merited is amply proven by the large audiences which have attended all of these lectures. The audiences are diversified in their nature, each lecturing topic calling for a select group of interested auditors. It is the intention of the College to continue annually similar series of popular science lectures.

PROMINENT CITIZENS ADDRESS THE STUDENT BODY ON CITIZENSHIP TOPICS.—A series of lectures on citizenship has been arranged for the benefit of the student body of the college. Men prominent in the promotion of civic and national betterment have been chosen to address the classes. Some of the lecture subjects are: "The Evolution of Government," "Municipal and State Political Organizations," "Democracy and the Individual Crowdmindedness," "Character as a National Asset."

AN EDUCATIONAL EXHIBIT.—The annual report of the National Museum of Washington, D. C., for the year ending June 30, 1921, devotes considerable space to the description of a biological exhibit of the H. K. Mulford Company products, recently installed in the Smithsonian Institute.

The article deals at length with Antitoxins and Vaccines for the prevention and cure of infectious diseases, all of which are illustrated in this unique exhibit.

The exhibit, which is the only display of biologicals in the museum, is located in the East Gallery. It comprises a number of cases containing specimens of Smallpox Vaccine, Diphtheria Antitoxin, Bactericidal Serums, Rabies Vaccine, Serobacterins, etc.

In addition to the specimens, photographs are shown of the various processes used in the Mulford Laboratories, also colored transparencies and charts.

The exhibit is strictly an educational one, and will prove of great value to physicians, pharmacists, nurses and other visitors.

Visitors to Washington should, by all means, endeavor to pay the exhibit a visit, as it is undoubtedly the most complete biological exhibit ever assembled, and one of the most attractive and interesting of educational exhibits in the institution.

BOOK REVIEWS

"Elements of Fractional Distillation." By Clark Shore Robinson. McGraw-Hill Book Co., Inc., 1922.

This volume in the International Chemical Series fills a place in the working library of the chemist who must give advice along engineering lines. Fractional distillation is discussed from the point of view of the Phase Rule, and from the standpoints of the production manager, the designer, and the manufacturer of such equipment. Forty-seven pages of tables and the corresponding bibliographies are given as an appendix; these tables contain a good deal of data not readily available. The author succeeds in dealing with the subject theoretically in a satisfactory manner while escaping the biases that sometimes follow such treatment. Thus on page 95, after arriving by theory at 45 as the proper number of plates to be used in a perfect column for separating benzene and toluene, he states, "A 45-plate column would, however, be excessively high for practical purposes, so under the circumstances, a shorter column would be used, say 36 plates." A few errors may be found by the careful reader, but they are not such as to reduce the usefulness of the book to an intelligent person. Thus on page 102, when discussing "Film Coefficient Water Side," when $V = 10.0$ ft. per sec., k_3

is given a value which is not the value that results from the formula supposed to have been used. This affects the value for $\frac{1}{K}$ in the center of the same page. Such errors are not surprising in the first edition of a detailed work.

In general, the book seems to be well adapted to use in practice as well as in detailed instruction in this branch of chemical engineering. The writer has given us a book that measures up to his stated intentions. It does not replace any older book known to the reviewer, but stands out as a unique contribution.

D. W. HORN.

OFFICIAL CATALOGUE OF STANDARDIZED PLANT NAMES IN PRESS.

All who buy, sell, handle, use, read about, or relate to plants, trees, shrubs, vines, seeds, or any horticultural subject in commerce, including every nurseryman, florist, seedsman, druggist, editor, author on plant topics, landscape architect, botanist, worker with plants, teacher about plants, and librarian, will constantly need to consult this Catalogue of Standardized Plant Names.

This great work, unique in character and usefulness, has been compiled and arranged by the American Joint Committee on Horticultural Nomenclature, made up of representatives appointed by the following organizations: American Association of Nurserymen, Ornamental Growers' Association, American Society of Landscape Architects, American Pharmaceutical Association, American Institute of Park Executives, and Society of American Florists and Ornamental Horticulturists.

ARRANGEMENT.

The plan of the Catalogue (which may run to 500 pages or more) is to include in the main alphabetical sequence the approved and synonymous scientific and common names of plants in American commerce, together with approved variety names of fruits, and complete lists of variety names in important classes such as rose, iris, etc.

Throughout, the approved scientific names are in **BOLD-face,** whether in capitals or small letters. Synonyms and unapproved

names are invariably in *italic*, either SMALL LETTERS or CAPITALS. Approved common and variety names are always in Small Capitals.

These typographic distinctions make the use of the catalogue easy, for the approved scientific name is always in Boldface, and the approved common name always in Small Capitals. The complete cross-indexing will facilitate finding approved names, directly or through synonyms.

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